DISEASES *of the* CHEST

VOLUME XII MAY-JUNE, 1946 NUMBER 3

Diasone in the Treatment of Pulmonary Tuberculosis*

EDWARD H. ROBITZEK, M.D., F.C.C.P.
GEORGE G. ORNSTEIN, M.D., F.C.C.P.
PHILIP SLATER, M.D., M.C.R.
STRASHIMIR A. PETROFF, Ph.D., Sc.D.
Staten Island, New York

The persistent and unrelenting search for a potent chemical agent in the treatment of tuberculous disease was given considerable impetus by the widespread acknowledgement and general acceptance of the sulfonamides in the treatment of numerous diseases of bacterial origin. That the known sulfonamide agents were proven to be unsatisfactory for clinical use in tuberculosis was recorded early and is generally known.[1,2,3] Continued studies, however, revealed that derivatives of 4-4′ diaminodiphenylsulfone produced an inhibitory effect on tuberculosis in guinea pigs.[3,4,5,6,7] The subject of the present report is one of these compounds, diasone,** the disodium formaldehyde sulfoxylate derivative of 4-4′ diaminodiphenylsulfone. This compound was synthesized by Raiziss[8] who produced it by the application of a known principle. Utilizing the technique underlying the conversion of arsphenamine to the less toxic neoarsphenamine by the introduction of the sodium formaldehyde sulfoxylate radical, he produced diasone from the mother substance diaminodiphenylsulfone by the introduction of a similar radical. Bauer and Rosenthal,[9] using different chemical methods, synthesized diasone almost simultaneously. The first and as yet unpublished reports of Petter and Prenzlau concerning the use of this agent in patients with pulmonary tuberculosis were sufficiently encouraging to warrant the current investigation. These workers subsequently published their findings[10,11] and their conclusions continued to indicate favorable results from the use of this drug.

*From the medical service of Sea View Hospital, Staten Island, N. Y.

**The diasone (the disodium formaldehyde sulfoxylate derivative of 4-4′ diaminodiphenylsulfone) was supplied through the courtesy of Dr. George R. Hazel of Abbott Laboratories, North Chicago, Illinois.

Copyright, 1946, by the American College of Chest Physicians.

Plan of Therapy and Choice of Cases

Upon initiating this study it was decided that a certain fundamental concept would have to be entertained. We felt that if this agent affected the tubercle bacillus either directly or indirectly the examination of the sputum would per force be the most important criterion of improvement. This neither implied nor sanctioned neglect of the other commonly employed criteria, but simply indicated that our opinion of diasone would be based directly upon its ability to kill or inhibit the growth of the organism. We further felt that the agent should be tested in a type of disease which neither tended toward spontaneous cure nor had attained the degree of advancement and velocity of progress which would render it entirely beyond the hope of control. For this reason the yardstick of the Ornstein, Ulmar, Dittler classification[12] was employed as being most satisfactory. Thus, patients were eliminated whose clinical histories, physical findings and x-ray manifestations indicated probable benign, resolving courses; those with caseous pneumonic or productive disease patterns were accepted. Our experience has amply shown that these latter patients, and particularly those in the caseous pneumonic group, evidence a marked tendency to progress if they remain untreated. Every effort was made, therefore, to eliminate the factor of fortuitous spontaneous healing.

The drug was administered with meals beginning at a dosage of one-third of a gram per day for one week, two-thirds of a gram per day throughout the second week and one gram per day for the succeeding weeks. It was administered in one-third gram capsules with 10 per cent sodium bicarbonate. Since the drug was potentially toxic, elaborate controls were established. Complete blood counts were performed twice a week for two weeks, once a week for the subsequent month, and once every two weeks thereafter. The urine was examined once a week throughout the entire test period. Diasone blood levels and sedimentation rates were determined once a week for two months and once every two weeks for the balance of the test period. These laboratory studies were supplemented by other procedures as indicated. Chest x-rays were taken in the AP and PA positions before institution of therapy and once a month for the balance of the course.

Each patient was chosen for the study at a medical conference after he had had a thorough work-up. This included history, physical examination, routine laboratory examinations including blood chemical studies, urine and Wassermann, x-rays of chest, electrocardiograms and determinations of the vital capacity with its relationship to the estimated normal. Evidence of extra-

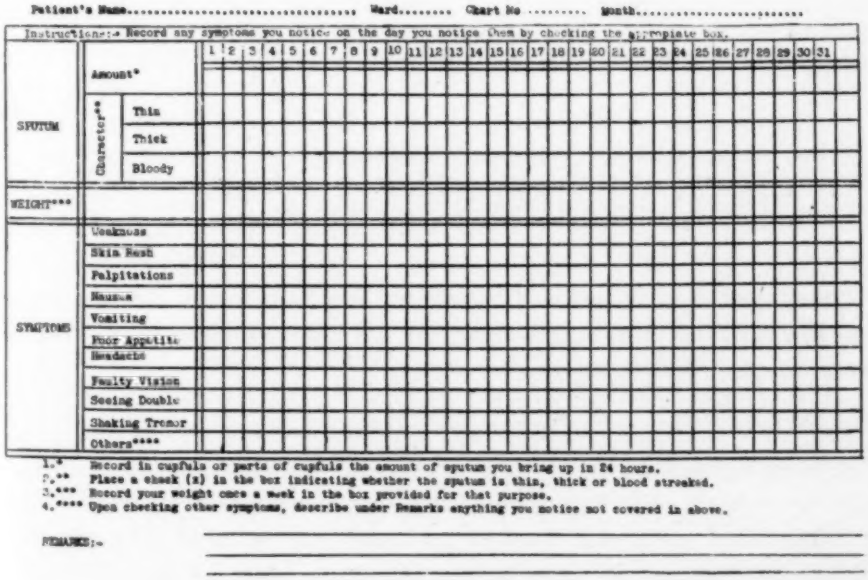
pulmonary tuberculosis, including empyema, other concomitant disease processes, hemoglobin concentrations of less than 70 per cent, advanced age or evidence of an unstable emotional state which might interrupt the treatment were considered sufficient cause for elimination of the patient from the series. No one was accepted whose sputum had not been persistently positive and none was accepted with pneumothorax. An arbitrary period of four months was initially decided upon as adequate for early evidence of improvement and each patient was asked to pledge himself for that period. He was given a mimeographed chart (Fig. 1) upon which he reported subjective observations including simple daily estimates regarding amount and character of sputum, weekly record of weight and such signs and symptoms as he, personally, might be expected to note and record. He was instructed to take bed rest but he was told to make no radical change from his previous habits.

His sputum was examined weekly with the plain direct smears being recorded from Gaffky I to X; the concentrated sputa and the concentrated gastric specimens were recorded as "few," "moderate," or "many" per slide. After two consecutive negative plain smears, concentrated sputa and concentrated gastrics were used exclusively.

Classification of Series Studied

A total of 106 patients appeared to be suitable and were selected by the medical conference for treatment. This group closely re-

FIGURE 1


Patient's Name..... Ward..... Chart No ..... Month.....

Instructions:- Record any symptoms you notice on the day you notice them by checking the appropriate box.

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
SPUTUM	Amount*																															
	Character** Thin																															
	Thick																															
	Bloody																															
WEIGHT***																																
SYMPTOMS	Weakness																															
	Skin Rash																															
	Palpitations																															
	Nausea																															
	Vomiting																															
	Poor Appetite																															
	Headache																															
	Faulty Vision																															
	Seeing Double																															
	Shaking Tremor																															
	Others****																															

1.* Record in cupfuls or parts of cupfuls the amount of sputum you bring up in 24 hours.
2.** Place a check (x) in the box indicating whether the sputum is thin, thick or blood streaked.
3.*** Record your weight once a week in the box provided for that purpose.
4.**** Upon checking other symptoms, describe under Remarks anything you notice not covered in above.

REMARKS:-

flects the proportions and character of the patient-population at Sea View Hospital.

Race:	White	71
	Colored	30
	Yellow	5
Sex:	Males	90
	Females	16
Age:	The youngest patient was 15 years of age, the oldest 57. The great bulk of the patients were between 20 and 35 years of age.	

Although we are entirely satisfied with our own classification of the cases chosen, in order to allow critical examination by those accustomed to other yardsticks, the series has also been classified in accordance with other standards:

Predominantly Caseous-Pneumonic	99
Predominantly Chronic-Productive	7
Total	106

Far-Advanced	68
Moderately-Advanced	35
Minimal	3
Total	106

Sputum positive 6 or more months before institution of therapy	80
Sputum positive less than 6 months before institution of therapy	26
Total	106

Sputum in high Gaffky range (V to X) before instituting therapy	79
Sputum in low Gaffky range (I to V) before instituting therapy	19
Sputum positive on concentrate or gastric only before instituting therapy	8
Total	106

Previous Thoracoplasty—Adjudged Unsuccessful	21
Previous Phrenic Avulsion—Adjudged Unsuccessful	1
Previous Cavernostomy—Adjudged Unsuccessful	1
Total	23

Many patients had had previous pneumothorax or bed rest therapy without appreciable benefit. No patient was accepted with residual pneumothorax.

Course and Toxicity

A wide variety of signs, symptoms and positive laboratory findings have been recorded. They were relatively mild and transitory, for the most part, and tended to disappear without altering the dosage or method of drug administration. Most of the reactions

occurred during the second month after which there was a rapid decline in incidence so that during the fourth, fifth and sixth months little of interest was reported. No correlations with the diasone blood levels could be made. The serious reactions are listed under "skin".

Therapy was discontinued because of toxicity in four of the 106 patients. These toxic side-reactions appeared in three colored and one Chinese patient; two of the colored were females. It is interesting to note that despite the fact that the white patients represented over two-thirds of the entire series, reactions severe enough to dictate discontinuance of the drug failed to appear in the white group.

We are reporting the complications in order of frequency.

Headache: This was the most commonly observed symptom having been reported on two or more occasions by 41 patients (39%). Never severe, it yielded to salicylates or cleared spontaneously.

Anorexia: The second most common complaint, noted by 39 patients (37%), was anorexia. It usually appeared at the beginning of the third month and continued throughout therapy. It was mild in degree.

Cyanosis: This was reported by the Ward Residents in 24 instances (22½%). It was noted early, appearing for the most part in the second or third weeks and gradually clearing spontaneously by the fifth or sixth week.

Nausea: Nausea appeared in 21 patients (20%). It was usually transitory and responded, in almost every instance, to closer adherence to the dictum that diasone capsules only be taken with substantial meals.

Tremor: Seventeen patients (16%) reported tremor. This symptom appeared most commonly during the third week and subsided at six or seven weeks. Usually mild in character, it rarely persisted beyond two and one-half months.

Vomiting: Of the 21 nauseated patients, 15 (14%) experienced some degree of vomiting. Rarely did this provide difficulty for control.

Weakness: Thirteen patients (12%) complained of a generalized weakness which had not been noted before therapy. This symptom too was mild and transitory.

Skin Lesions: Of the reactions sustained, skin lesions were invariably most serious. All four patients from whom diasone had to be withdrawn displayed some type of skin lesion. They are classified as follows:

1) A 21 year old colored female had the onset of a maculopapular eruption which rapidly assumed a pemphigoid character.

This proceded to a fatal termination and has been reported elsewhere.[13]

2) A 56 year old Chinese male had the onset of a toxic erythema associated with high temperature and marked toxicity. The lesions subsided 10 days after drug discontinuance. Diasone was not resumed.

3) A 54 year old colored male with a far-advanced caseous-pneumonic tuberculous pulmonary disease had persistent nausea, vomiting and epigastric pain associated with a maculo-papular rash over both forearms. The symptoms subsided with drug discontinuance.

4) A 31 year old colored female developed an acute hepatitis characterized by a large, tender liver and jaundice and associated with generalized lymphadenopathy and a widespread maculo-papular eruption. These lesions subsided with drug discontinuance and routine supportive therapy. Subsequent bromsulphalein and cephalin floculation tests have failed to demonstrate evidence of permanent liver impairment.

Including these four more serious reactions, skin lesions were noted 10 times (9.4%). They varied from urticarial lesions and dry, scaly exfoliations to the pemphigoid type noted above. In addition to these permanent drug discontinuances, diasone was stopped completely and resumed in two instances, reduced and resumed in three and continued despite lesions in three. No permanent lesions or pigmentary changes have been noted.

Palpitations: Seven patients (6½%) complained of momentary palpitations. Since this was a subjective complaint and never seen by a member of the staff we feel that the most probable explanation is that these were extra-systoles. In but two of these patients was there a repetition of this symptom.

Tachycardia: Temporary elevations of pulse rate to 120 or 130 were noted in six patients (5.7%). These elevations appeared suddenly and subsided without therapy in one to two hours. None was noted after the second month of therapy.

Epigastric Pain: In mild or moderate degree this was noted five times (4.7%) and again, strict adherence to the rule that no diasone was to be taken without food modified or eliminated this symptom.

Visual Disturbances: Four patients (3.8%) volunteered that they had had visual disturbances. Each complained of eye fatigue with protracted concentration upon printed matter but insisted that he had not noted this disturbance before. It was no longer noted after the third month. No patient admitted to diplopia.

Streaking: Streaking occurred in four patients (3.8%). In one

it was brisk. This is about the incidence expected in a group of this size with this type and character of pulmonary disease.

Nervousness: Three patients complained of excessive nervousness (2.8%). It was independent of tremor but followed the same course, clearing within two months without alteration of therapy.

Polyphagia: Two patients (1.9%) stated that their appetites had become voracious. Both of these patients later complained of anorexia.

The following signs and symptoms were noted once each: Tinnitus, nose bleed, constipation, dyspnoea, hepatitis, jaundice, lymphadenopathy, insomnia.

Despite efforts to eliminate extraneous features it is conceded that diasone may not have been responsible for many of the above signs and symptoms. It is in the nature of subjective observations that this should be so. The following, however, are laboratory findings and somewhat less disputable.

Urine: Complete urine examinations revealed the presence of albumin in the urines of 66 of 106 patients (62%). This varied from a "faint trace" to "two plus" and was present from one to eighteen times in the same patient. Occasional hyaline and granular casts were seen in ten of these patients and "occasional" red blood cells in three others. Neither casts nor red cells were persistent and renal function tests failed to show other evidence of damage. Since patients with a history of albuminuria were eliminated at the preliminary medical conference it cannot be denied that this finding was a concomitant of therapy. The subsequent observation time has been too short to attest to the permanency of this condition. However, early impressions suggest that it is transitory.

Blood: Our positive blood findings are limited to the red blood cell counts and hemoglobin concentrations (Hellige Wedge Hemometer —16.6 Gms. Hgb. /100 cc. blood = 100%). Abrupt drops in both components were noted with the low point usually being reached between the second and fourth weeks. One hundred and four of the 106 patients experienced some degree of drop in hemoglobin and red blood cell count. The average hemoglobin loss was 13.51% (3.375 Grams Hgb. /100 cc. blood), and the average red blood cell loss was 714,000 cells. The greatest drop was 27% hemoglobin (6.75 Gms. Hgb. /100 cc. of blood) (five patients) and 1,490,000 red blood cells (one patient). At four months 69 patients showed a secondary rise, which averaged 9.6% Hgb. (2.4 Gms. Hgb. /100 cc. of blood) and 448,000 red blood cells (70 patients). At four months, 58 patients were dropped from diasone therapy (including the four dropped earlier because of toxicity). During the subsequent two months the remaining 44 patients received

six grains of ferrous sulphate per day. These experienced an average rise in hemoglobin values of 12.1% (3.025 Gms. Hgb. /100 cc. of blood) and 671,000 red blood cells. At the end of the 6 month period 90 patients of the original 106 patient series were still available for examination. They demonstrated an average rise of 11.21% Hgb. (2.8 Gms. Hgb. /100 cc. of blood) and 642,400 red blood cells. The 44 continuing treatment, it will be noted, had an average greater red blood cell recovery than the combined group. We feel that this was due only in part to the adjunctive iron therapy; in part it seemed due to the fact that the additional two months was only offered to the patients who seemed to derive some benefit from the treatment. Thus a selective process was operating wherein the less favorable cases were dropped.

Careful scrutiny of the leucocytes failed to reveal persistent changes in this element of the blood count. In addition, we were unable to demonstrate any alterations in the lymphocyte-monocyte ratio. Furthermore, leukopenia did not occur. In each instance the total count, its differential and the cellular morphology mirrored the patient's clinical condition in the expected fashion. We do not feel that diasone had altered the white cell series in our cases.

Temperature: Temperature records failed to demonstrate changes which could be attributed directly to the use of diasone.

Blood Diasone Levels

The blood levels were repeatedly determined in an effort to correlate therapeutic efficacy or toxicity with the blood concentrations. This was disappointing since no correlations were established. No attempts were made to obtain unusually high levels through the use of high diasone dosages and the recommended gram per day was continued in each case. In general, the blood level reached its peak at the end of the first month and subsequently fell off slowly to low levels. The blood was uniformly taken at a specified time of the day and the determinations were immediately performed by a competent chemist. In several instances there was incontestable evidence that the patient was indeed taking his medication and there were clinical indications of toxicity (cyanosis, tremor, nausea, etc.), despite which, levels of "zero" or "trace" were reported. In these cases, chemical examination of the urine always revealed the presence of diasone, due in all probability, to concentration by the kidney. We furthermore failed to note any correlation between body volume and blood level and attempts to establish a relationship between albuminuria and the blood level were invariably unavailing. The average level was .438 mgs. per

cent. Highs of "just over 3.0 mgs. per cent" were occasionally encountered and readings of "zero," were frequent.

Results

After four months of continuous diasone therapy the patients were brought back to the medical conference for preliminary evaluation. Those failing to exhibit any evidence of improvement were dropped from the series. As anticipated, the problem of determining "improvement" was complicated by the difficulty in temporarily setting aside the generally accepted criteria of such improvement. We were entirely aware of the portentiousness of an increased appetite, a rising weight curve and a clearing x-ray, but we felt that if we were to hew to our concept of sputum conversion as the primary desideratum, we must reject the tendency to allow these elements their usual import. Furthermore, since we knew we were dealing with a drug potentially toxic to both host and microorganism, we felt we must anticipate sputum conversion in the face of generally regressive changes. These would result from the continued use of a noxious agent. Indeed, it seemed likely that the so-called "open healing" phenomenon might be encountered; that is, persistence of cavitation despite other evidence of an arrested state. We have occasionally seen cases of this character and have been able to demonstrate pathologically that these cavity walls are smooth and shiny and are lined by squamous epithelium. Auerbach[14] has demonstrated this phenomenon particularly well and has emphasized its frequency in well-drained post-cavernostomy cases. This suggests that anything which will destroy or alter the tubercle bacillus implantations within the cavity wall will allow rapid epithelial overgrowth before cavity closure can occur. We firmly believe that this type of healing will be common when the appropriate agents or modalities are employed.

Sputum: Significant changes in the amount or character of the sputum did not occur in any instance. The minor variations invariably mirrored the clinical courses and were never remarkable.

We have listed our patients in regard to alteration of sputum, labeling many of them "conversions". We concede that a four-month period of observation with two or three months of sputum negativity cannot rightly be called "conversion". However, for purposes of early classification, patients whose sputa had been persistently positive before therapy but who later produced a series of negative concentrates were considered "converted". Similarly, we arbitrarily labeled patients whose sputa had been significantly reduced from high Gaffky values to "positive on concentrate or concentrated gastrics only," as "reduced".

Total Series for Evaluation of Therapy	102 Patients
Conversion	20 (19.6%)
Reduced	15 (14.7%)
No change	67 (65.7%)

These are classified as follows:

"Conversion" in patients persistently positive 6 or more months before institution of therapy	12	(15.8% of the 76 patients in this category)
"Conversion" in patients positive less than 6 months before institution of therapy	8	(31% of the 26 patients in this category)
Total	20	
"Reduction" in patients persistently positive 6 or more months before institution of therapy	11	(14.5% of the 76 patients in this category)
"Reduction" in patients persistently positive less than 6 months before institution of therapy	4	(15.4% of the 26 patients in this category)
Total	15	
"Conversion" from high Gaffky (V to X)	9	(12% of the 75 patients in this category)
"Conversion" from low Gaffky (I to V)	6	(31.5% of the 19 patients in this category)
"Conversion" from concentrate	5	(62½% of the 8 patients in this category)
Total	20	
"Reduction" from high Gaffky	8	(10.6% of the 75 patients in this category)
"Reduction" from low Gaffky	7	(36.8% of the 19 patients in this category)
Total	15	
"Conversion" from predominantly caseous pneumonic	17	(17.9% of the 95 patients in this category)
"Conversion" from predominantly productive	3	(43% of the 7 patients in this category)
Total	20	

"Reduction" from predominantly caseous pneumonic	14	(14.7% of the 95 patients in this category)
"Reduction" from predominantly productive	1	(14.3% of the 7 patients in this category)
Total	15	
"Conversion" from far-advanced	10	(15.6% of the 64 patients in this category)
"Conversion" from moderately advanced	9	(25.7% of the 35 patients in this category)
"Conversion" from minimal	1	(33 1/3% of the 3 patients in this category)
Total	20	
"Reduction" from far-advanced	6	(9.4% of the 64 patients in this category)
"Reduction" from moderately advanced	9	(25.7% of the 35 patients in this category)
Total	15	

Of considerable interest is the observation that among these 20 "conversions" there are nine patients who had had thoracoplasties. The thoracoplasties had failed to convert the sputum. These nine are classified as follows:

Total number of post-thoracoplasty patients	21	
Evidence of conversion	9	(42.6%)
Of these 9, cavity visualized tomographically	4	
Cavity not visualized tomographically	5	
	9	

Of additional interest is a combination of "conversion" and "reduction" figures in the total tabulations. We are acutely aware that the traditional yardsticks give little place to the "reduced" sputum even though experience has shown that the Gaffky X sputum is more dangerous to patient and environment than is the "positive, few per slide," on concentration. The majority of clinicians will only accept the negative sputum as indicative of improvement. But since this study is predicated upon the concept of "sputum conversion due to chemotherapy," we may safely allow ourselves the preliminary speculations that patients with significantly reduced sputum bacillary counts are indeed improved. Combining the two groups then, we have the following:

Total	102
Improved (combined "conversion" and "reduction")	35 (34.3%)
No change	67 (65.7%)

This suggests that at four months, one-third of the treated group appeared to derive some benefit from diasone therapy.

Of the entire 102 patient series, 44 were requested to continue diasone therapy for another two month period. In addition to the 35 patients showing improvement in sputum, nine showed sufficient improvement in other directions to make further study under therapy worth while. Three of the 44 refused to continue treatment. One of these three had been listed as a probable conversion, two as reductions. (A three month follow-up on the former continues to demonstrate persistence of the sputum negativity and a similar follow-up on the latter indicates a similar persistence of the reduction). Thus, of the 41 remaining patients completing the six month course, there were 19 listed tentatively as "conversions" and 13 as "reductions".

The six-month tabulation for this 41 patient group follows:

Series	41 patients
Conversion	8 patients
Reduction	19 patients
No change	14 patients

The tabulation at six months for the entire 102 patient series, including the unbenefited group dropped at four months, presents the following:

Total series	102 patients
Conversion	9 (8.8%)
Reduction	21 (20.6%)
No change	72 (70.6%)

This, on comparison with the four month findings, shows that the "conversion" group has fallen off from 20 patients (19.6%) to 9 (8.8%), and the "reduction" group has risen from 15 patients (14.7%) to 21 (20.6%).

In addition, it is to be noted that three of the original "converted" cases have resumed high Gaffky levels and eight have entered the "reduced" group. Two "reduced" resumed high levels.

Weight: Patient's weights were recorded once a week throughout the entire test period. Analysis of the entire group undergoing the minimum course of therapy and computed at its conclusion reveals the following:

37 patients gained weight.
52 patients lost weight.
13 patients remained stationary.

Average weight gain was 5.03 pounds.
Average weight loss was 5.35 pounds.

The greatest weight gain in any one patient was 12 pounds.
The greatest weight loss in any one patient was 12 pounds.
We feel that there is nothing significant in these figures.

Sedimentation Rate: These rates, as noted, were checked at frequent intervals. The following record covers the entire 102 patient series during the period of chemotherapy.

Using the Westergren apparatus the sedimentation rate was reported in millimeters of drop in one hour.

The sedimentation rate dropped	in 72 patients
The sedimentation rate rose	in 23 patients
The sedimentation rate was unchanged	in 7 patients

The average fall was	12.25 mm.
The average rise was	8.22 mm.

The greatest drop was	46 mm.
The greatest rise was	30 mm.

We do not feel that these figures are significant since similar changes are to be expected in any group of tuberculous patients under similar conditions.

X-Ray: We have deliberately minimized the importance of the x-ray as a criterion of improvement since, as we have stated, our concept of chemotherapeutic cure in tuberculosis revolves about control of the organism. If, then, such control were to be established, one would per force anticipate an appreciable lag between the time of destruction of the bacillus and a change in the x-ray pattern.

For the sake of completion, however, and in order to retain a continuity of observation, AP and PA films were taken before therapy was instituted and monthly thereafter. Whenever indicated, tomographs or other studies were made.

The serial roentgenographic observations were approximately those to be expected in any group of tuberculous patients comparable in size and character. Over half (54) went through the full course of therapy without appreciable x-ray changes. Another group (18), as might be expected, demonstrated minimal to moderate clearing of infiltrate. In four instances there was an appreciable reduction in cavity size. Among the unfavorable observations we noted new infiltrates on one or both sides in 17 patients and increased cavity size in 21. New cavities were noted twice and in one instance a pleural effusion appeared and reabsorbed during the course of therapy. This is in contrast to Petter and Prenziau's report which states that "bronchogenic spread of the disease did

not occur."[11] This, presumably, implies that no new infiltrates were noted during the period of therapy. In our series, diasone did not prevent spreads. A breakdown of the x-ray findings among the nine cases with converted sputa showed moderate clearing of infiltrate in three and no observable change in six. In only one of these cases was there a clearly visible cavity before the institution of therapy and in this instance the cavity outline remained clearly visible despite the clear-cut production of sputum negativity.

Controls

In any statistical study regarding the evaluation of a therapeutic agent the question of a suitable control series is raised. In this study it was originally felt that such a series would be unnecessary since we knew from experience that any group of patients of the type chosen would show approximately a ten per cent spontaneous sputum conversion rate. We felt that we should only accept unequivocal results if this drug were to achieve standing as a worthy member of the sulpha-drug family. Since, however, others might question the validity of this experience, we have examined the sputum records of 50 patients who were originally passed for diasone treatment by the medical conference but who were subsequently rejected for one of the following reasons: 1) Patient didn't wish to be treated, 2) patient refused to pledge himself to four months continual therapy, 3) patient was psychologically unsuitable, 4) patient's vital capacity was too low (below 50 per cent of estimated normal), 5) patient's hemoglobin was too low (70% was the lowest concentration accepted) borderline cases were rejected. At the conclusion of six months of conservative therapy, this control group showed a sputum conversion rate of 12 per cent and a reduction rate of four per cent. We accept these as the usual rates.

Discussion

We believe it fitting to open this discussion by quoting from Dr. M. Pinner's Editorial, "Evaluation of Chemotherapy."[15] "The proper patients for such studies are those with relatively early lesions, either clinically incipient foci or early secondary (bronchogenic) lesions whose data of first development is known." We cannot fully agree with this concept since the prognosis of "relatively early lesions" is notoriously unpredictable. The true pathological natures of these lesions are frequently misinterpreted during the initial phases and, in consequence, it is not unusual for a full 50 per cent or more of this group to be composed of resolving exudative lesions. Since resolution, irrespective of geog-

raphical extent, is the characteristic bent of such lesions, one may anticipate brilliant results with any therapeutic measure. Indeed, as our controls have indicated, there is even a 12 per cent spontaneous conversion rate among the malignant caseous-pneumonic lesions. It is therefore mandatory to demonstrate an appreciably greater than 12 per cent cure rate in this group in order to lay claim to the therapeutic efficacy of any agent. We emphasize this point since we feel that useful therapeutic agents should produce conclusive results; if they are borderline, they are probably worthless.

Our results clearly indicate that diasone does not cure chronic pulmonary tuberculosis in human beings. That it favorably affects the course of tuberculous disease in guinea pigs seems beyond dispute as Feldman, Hinshaw and Moses,[6] Callomon,[4] Callomon and Groskin,[3] and Smith, Emmart and Stohlman,[5] with somewhat less enthusiasm, have shown. What, then, is responsible for this difference? We do not believe comparisons of the disease patterns in guinea pigs and humans may be lightly made. The acute, vascular lesions of guinea pigs are not to be closely compared with the relatively avascular and chronic lesions of the human. Actually, as a direct result of these vascularity factors, it is not inconceivable that adequate concentrations of diasone never achieve active contact with the cavitary and pericavitary tissues. A final evaluation of this drug must await such a demonstration.

Furthermore, we should like to call attention to the relative discrepancies between the dosages of diasone employed in humans and experimentally in guinea pigs. Dosages fed to pigs vary from 200 milligrams per animal per day (Callomon[4]) to 325-350 mgs. per animal per day (Feldman, Hinshaw and Moses[6]). Animal weights are not recorded by all observers but they appear to vary from 250 grams (Smith, Emmart and Stohlman[5]) to an average of 486 grams (Giroux[7]). Relative to a 150 pound patient this would indicate diasone dosages of 30 to 50 grams per day; in short, 30 to 50 times the average clinical dose. It may be argued that the blood levels obtained in guinea pigs by these investigators were rarely beyond five mgs. per cent (Callomon and Groskin[3]) but, as we have pointed out, the blood levels are disappointing clinical indices of saturation. We doubt if anyone would risk the high dosages apparently called for in the guinea pig studies.

It might be well at this point to also call attention to the lack of uniformity in the tubercle bacillus strains used and the wide variations in the dosages employed by the various investigators in infecting their animals. Standard strains are used; but often strains taken haphazardly from patients with tuberculosis are employed without particular regard to degree of virulence. Sim-

ilarly dosages are noted to vary from one-two thousandth of a milligram (Feldman, Hinshaw and Moses[6]) to two milligrams (Callomon[4]). Would not the clinician be less misled by the standardization of some of these factors?

One curious feature demands comment. At four months the sputum conversion rate, particularly among the post thoracoplasty cases, appeared to presage an excellent six month tally. That this was not forthcoming, we have shown, and indeed, the results were substantially less favorable than those of the control group. We have pointed out that of the 20 patients suggestively converted at four months, 11 resumed a state of positivity and three of these 11 returned to high Gaffky levels. Similar circumstances were not observed among the controls nor has it ordinarily been our experience to note relapses in such a high percentage of apparently improving patients. One explanation immediately suggests itself. Sputum conversion in chronic pulmonary tuberculosis is almost invariably associated with cavity closure. This fact has often been noted roentgenographically and is universally accepted. We were not impressed by the occurrence of this phenomenon in our cases in spite of the fact that 20 of them were producing negative sputa at four months. Since, however, we are now dealing with another mechanism, "chemical sterilization" of the cavity without closure, the probability that diasone exerted early control is given greater credence. It appears, then, that diasone exhibited an early effect of a desirable nature but later lost its grasp. Also noteworthy in this regard is the observation that at four months 34.3 per cent of the patients had sputa which were either "converted" or appreciably reduced and the bulk of these patients, as we have shown, came from the lower Gaffky, predominantly productive, minimal or moderately advanced groups. Although we again tread in the realm of spontaneous cure, the suggestion cannot be avoided that this drug exerts some effect when the infection is not entirely overwhelming. This also provides grounds for the supposition that the mechanism of drug fastness may be operating. We have not proven the validity of this supposition, but suggest that culture studies may clarify the issue. The patients experiencing these sputum relapses are being followed closely in an effort to disentangle this problem.

In view of the rapid chemotherapeutic advances and in view of the probability that tuberculosis will liberally partake of these benefits, we believe it should be emphasized that these new concepts will have to be held in the classifications of treated patients. Thus it will no longer be sufficient to label patients "arrested" or "apparently arrested" on the basis of a period of negativity since we do not know whether the chemotherapeutic agent has destroyed

the organism or merely inhibited it. This will require a great deal of study.

Despite our final tabulations we do not feel that diasone should be dropped. Rather, it is the direction of investigation that requires alteration. This conclusion is based in part upon the reported guinea pig results and in part upon our own observations which seem to show that diasone in some esoteric manner alters the life history of the tubercle bacillus without causing his demise We feel that further investigation is justified.

SUMMARY

1) A concept of chemotherapeutic cure in tuberculosis is entertained whereby sputum alteration becomes the major criterion of change.

2) Cases benignly resolving or inevitably progressive and those complicated by extra-pulmonary tuberculosis or other diseases were eliminated from this study in order to fairly evaluate the usefulness of diasone.

3) One hundred and six patients were selected for the study. Ninety-three per cent of these were classified as predominantly caseous-pneumonic. According to other classifications, they are recorded as 64 per cent far-advanced, 33 per cent moderately advanced; 75 per cent were positive over six months before institution of therapy; 75 per cent had sputa in the high Gaffky range.

4) Therapy was discontinued in four of the 106 patients because of marked toxicity. There were skin lesions in each of these cases; one terminated fatally. Other signs and symptoms of toxicity were frequently encountered but these were relatively mild and transitory.

5) Results after four months of therapy — 102 patients.

Evidence of conversion in 20 patients (19.6%); sputum appreciably reduced (See text, "sputum" under heading of "results" for definition of "reduction") in 15 patients (14.7%). The conversions and reductions occurred at a higher rate in the moderately advanced or minimal, predominantly productive groups and in those positive less than six months before institution of therapy.

6) The combined conversion and reduction rate was 34.3 per cent.

7) Results after six months of therapy — 41 patients.

Evidence of conversion in eight patients, appreciable reduction in 19. Total combined tabulation of the entire 102 patient series indicates sputum conversion in nine patients (8.8%), appreciable reduction in 21 (20.6%).

8) The chest x-ray demonstrated no significant change in one-half of the series. There was clearing and reduction in cavity size in one-fifth of the series; new lesions and increased cavity size were

noted in one-fifth; new cavities appeared in two patients. Among the conversions there was clearing in one-third of the patients and no change in two-thirds. One conversion presented a persistently visible cavity. Diasone did not prevent spreads. Emphasis is placed upon the relative unimportance of the x-ray in evaluating chemotherapy since considerable lag between "sterilization" and visible healing changes is anticipated.

9) A 50 patient control series manifested 12 per cent spontaneous conversion and four per cent reduction rates.

10) The unusually high percentage of relapses at six months after an excellent start at four months suggests interference with the proliferation of the tubercle bacillus at that time and reflects the probability of early "open healing." It also introduces the concept of "drug fastness."

11) With chemical control of the tubercle bacillus the usual criteria of arrest will have to undergo considerable modification.

12) Because of the evidence of early weak activity, diasone should not be abandoned but a new approach should be considered.

RESUMEN

1) Se propone un concepto de curación quimioterapéutica de la tuberculosis en el que se considera la alteración del esputo el criterio más importante del cambio.

2) En este estudio fueron eliminados los casos benignos resolventes o inevitablemente evolutivos y aquellos complicados por tuberculosis extrapulmonar u otras enfermedades, a fin de apreciar justamente la utilidad de la diasona.

3) Se seleccionó a 106 enfermos para este estudio. Se clasificó como predominantemente caseoneumónicos al 93 por ciento de ellos. De acuerdo con otras clasificaciones, el 64 por ciento estaban muy avanzados, el 33 por ciento moderadamente avanzados; el 75 por ciento habían sido positivos por seis meses antes de la iniciación del tratamiento; el 75 por ciento tenían esputos con altas cifras en la escala de Gaffky.

4) Se suspendió la terapia en cuatro de los 106 enfermos a causa de marcada toxicidad. Sobrevinieron lesiones cutáneas en cada uno de estos casos; uno de ellos tuvo un desenlace fatal. Frecuentemente aparecieron otros signos y síntomas de toxicidad, pero éstos fueron relativamente leves y transitorios.

5) Resultados después de cuatro meses de tratamiento—102 enfermos.

Prueba de conversión en 20 enfermos (19.6%); esputo reducido apreciablemente (Véase en el texto "esputo," bajo el título de "resultados," para la definición de "reducción") en 15 enfermos (14.7%). Las conversiones y reducciones ocurrieron en una pro-

porción más elevada en los grupos moderadamente avanzados o mínimos y predominantemente productivos, y en los que habían sido positivos menos de seis meses antes de iniciar la terapia.

6) La proporción de conversiones y reducciones combinadas fue de 34.3 por ciento.

7) Resultados después de seis meses de tratamiento—41 enfermos.

Prueba de conversión en ocho enfermos, reducción apreciable en 19. Recapitulación total combinada de la entera serie de 102 enfermos indica conversión del esputo en nueve enfermos (8.8%), reducción apreciable en 21 (20.6%).

8) La radiografía torácica no demostró ninguna alteración significativa en la mitad de la serie. Hubo resolución y reducción en el tamaño de la caverna en una quinta parte de la serie; se notaron nuevas lesiones y aumento en el tamaño de la caverna en otra quinta parte; aparecieron nuevas cavernas en dos enfermos. Entre las conversiones tuvo lugar la resolución en una tercera parte de los enfermos y no hubo alteración en dos terceras partes. Una de las conversiones presentó una persistente caverna visible. La diasona no evitó propagaciones. Se hace hincapié sobre la relativa poca importancia de la radiografía en la apreciación de la quimioterapia, puesto que se anticipa que ha de pasar un período de tiempo considerable entre la "esterilización" y visibles alteraciones de cicatrización.

9) En una serie de 50 enfermos que sirvieron de testigos el 12 por ciento manifestó conversión espontánea y el 4 por ciento reducción del esputo.

10) El porcentaje excepcionalmente elevado de recaídas a los seis meses, después de un excelente comienzo a los cuatro meses, indica que la droga interrumpió la reproducción del bacilo tuberculoso en el corto tiempo y refleja la probabilidad de "cicatrización abierta" temprana. Ello también introduce el concepto de "droga resistencia".

11) Con el control químico del bacilo tuberculoso el criterio usual del estacionamiento tendrá que ser modificado considerablemente.

12) Debido a la evidencia de que la diasona manifiesta una actividad temprana, aunque débil, no debe abandonársela sino considerársele un nuevo abordaje al problema.

REFERENCES

1 Rich, A. R., and Follis, R. H., Jr.: "The Inhibitory Effects of Sulfanilamide on the Development of Experimental Tuberculosis in the Guinea Pig," *Bull. Johns Hopkins Hosp.*, 62: 77, 1938.
2 Buttle, G. A. H., and Parish, H. J.: "Treatment of Tuberculosis in Guinea Pigs with Sulphanilamide," *Brit. M. J.*, 2: 776, 1938.
3 Callomon, F. F. T., and Groskin, L.: "Therapeutic Effect of Some New

Derivatives of Di-amino-diphenyl Sulfone in Experimental Tuberculosis of Guinea Pigs," *Tuberculology*, 7: 21, (Feb.) 1944.
4 Callomon, F. F. T.: "New Derivatives of Diaminodiphenylsulfone—Their Therapeutic Effect in Experimental Tuberculosis of Guinea Pigs," *Amer. Rev. Tuberc.*, 47: 97, 1943.
5 Smith, M. I., Emmart, E. W., and Stohlman, E.: "The Action of Some Derivatives of 4-4' Diaminodiphenylsulfone in Experimental Tuberculosis," *Am. Rev. Tuberc.*, 48: 32, 1943.
6 Feldman, W. H., Hinshaw, H. C., and Moses, H. E.: "Therapeutic Effects of Disodium Formaldehyde Sulfoxylate Diaminodiphenyl Sulfone in Experimental Tuberculosis," *Arch. Path.*, 36: 64, 1943.
7 Giroux, Maurice: "Traitement de la Tuberculose Expérimentale du Cobaye," *Laval Médical*, 9: 788, (Décembre) 1944.
8 Raiziss, G. W.: "Diasone, A New and Active Chemotherapeutic Agent," *Science*, 98: 350, 1943.
9 Bauer, H., and Rosenthal, S. M.: "Studies in Chemo-therapy. VII. Some New Sulphur Compounds Active Against Bacterial Infections," *Pub. Health Rep.*, 53: 40, 1938.
10 Petter, C. K., and Prenzlau, W. S.: "Diasone (diaminodiphenyl sulfone derivative); Clinical Application in Human Tuberculosis; 8 Months Study," *Ill. M. J.*, 85: 188-197, (Apr.) 1944.
11 Petter, C. K., and Prenzlau, W. S.: "Treatment of Tuberculosis with Diasone," *Amer. Rev. Tuberc.*, 308-322, (Apr.) 1944.
12 Ornstein, George G., Ulmar, David, and Dittler, Edgar L.: "A Clinical Classification of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 23: 3, 1931.
13 Robitzek, E. H.: "Fatal Pemphigoid Reaction to Diasone," *Am. Rev. Tuberc.*, LI: 5, 473-7, (May) 1945.
14 Auerbach, O.: "The Pathology of Clinically Healed Tuberculous Cavities," *Am. Rev. Tuberc.*, 707-730, (Dec.) 1940.
15 Pinner, M.: Editorial— "Evaluation of Chemotherapy," *Am. Rev. Tuberc.*, 257, (Sept.) 1944.

Dyspnoea and Diminished Vital Capacity as a Symptom and a Sign in Hay Fever

ETHAN ALLAN BROWN, M.D., F.C.C.P., M.R.C.S. (London), L.R.C.P. (England), F.A.C.A.*
CONRAD NOBILI, M.D., F.A.C.A.**
THEODORE SANNELLA, M.D., Ph.G.***
GEORGE P. WADSWORTH, Ph.D.****
Boston, Massachusetts

The present paper concerns itself with the diminution of vital capacity observed during the pollen season in patients with either uncomplicated hay fever or pollen asthma. Although the diminution of vital capacity of patients with bronchial asthma has been carefully studied by a number of workers, the Cumulative Index, as far as can be discovered, contains no reference to the relationship between vital capacity and pollen hay fever.

From a clinical point of view, it was observed by one of us (EAB), during the ragweed pollen season of 1940, that many of the patients with hay fever appeared to be unusually dyspnoeic after they had climbed the two flights of stairs to the Allergy Clinic of the Boston Dispensary. Interrogation elicited the fact that many of the patients had previously noted breathlessness on exertion during the hay fever season, but ascribed their dyspnoea to their nasal stenosis and forced mouth breathing. It was, of course, obvious that the facts fitted an exactly opposite conclusion since dyspnoeic patients breathe through their mouths although the nasal passages are clear.

From the physiological point of view, the mucous membrane of the respiratory tract is continuous from the nasal vestibule to the final pulmonary alveoli; and it was only logical to assume that a sensitivity to pollen would not necessarily be limited to that portion of the mucosa bounded by the upper respiratory passages. It is also evident that patients suffering from nasal stenosis, and breathing orally, are unable to filter their air as do those breathing nasally. Pollen and other particles are therefore more easily deposited in the lungs. It has long been known that nasal irritation may cause reflex spasm of the bronchial musculature.

---

*Physician-in-Chief, Department of Allergy, New England Medical Center, Boston, Massachusetts.
**Assistant, Department of Allergy, New England Medical Center, Boston, Massachusetts.
***Assistant, Department of Allergy, New England Medical Center, Boston, Massachusetts.
****Massachusetts Institute of Technology, Cambridge, Massachusetts.

From a pathological point of view, it has often been observed that a good number of patients with untreated hay fever develop pollen asthma. It is also a clinical fact that some patients with pollen sensitivity manifest allergic coryza early during the pollen season, and bronchial asthma later; although there are patients whose first symptoms of pollen sensitivity occur as bronchial asthma, and others in whom the allergic coryza is, in later years, entirely replaced by bronchial spasm and bronchial mucous-membrane edema.

During the pollen seasons of 1941, sixty-two patients were studied from late in May until early in October. This data was admitted to one of us (GPW). The records did not extend sufficiently long before or after the pollen season to be acceptable statistically. None of the records of the first patients were used for the present paper. For the pollen season of the next year, 1942, forty-two patients were studied from early April to late October, and in some cases to early December. The data was kept for two years in order to discover whether or not the facts elicited could be used as an index of prognosis in patients suffering from pollenosis.

Of these forty-two patients, eighteen had simple uncomplicated hay fever due to ragweed pollen sensitivity. There were no other significant sensitivities and minor symptoms, if any, extra-seasonally. The remaining patients in the series were chosen in order that certain conditions might be fulfilled, and that they might serve as a "running control". There was one group chosen whose pollen sensitivities were sequential, as due to timothy and ragweed; and others whose pollen sensitivities were multiple, the seasons for which were coincidental and perhaps acting cumulatively. A number of patients had extra-seasonal or environmental sensitivities. The patients can therefore be classified in the following categories.

Five patients presented a picture of seasonal pollen hay fever associated with clinical, perennial dust sensitivity. They did not suffer from bronchial asthma.

Two patients presented symptoms of seasonal ragweed pollen hay fever, associated with occasional wheezing during the ragweed pollen season.

As controls, three patients with typical bronchial asthma, due to ragweed pollen sensitivity, were chosen. These suffered from occasional slight symptoms, perennial in type, due to an associated dust sensitivity.

Two patients presented the picture of hay fever and bronchial asthma due to seasonal pollen sensitivity, with marked symptoms occurring perennially and due to house dust.

One patient suffered from timothy, ragweed, and dust coryza;

and another with parallel sensitivities, due to the same pollens and dust, responded with bronchial asthma.

Of the remaining patients, one was a simple, uncomplicated timothy hay fever; one was sensitive to timothy and plantain; and a third to plantain and ragweed. One patient presented clinical symptoms of timothy, plantain and ragweed sensitivity. Another proved sensitive to birch, oak, timothy and ragweed pollens.

The last three patients in the series presented nasal symptoms due in the first to birch, oak and ragweed sensitivities; in the second to birch, timothy and ragweed pollens; and in the third to timothy, feathers and dust. In this latter group of nine patients, none had ever suffered from bronchial asthma.

The patients were purposely chosen from these typical groups since those with hay fever whose symptoms came early in the Spring could be studied during the Summer and the Fall, while free of symptoms; those who manifested symptoms during the Fall could be studied during the Spring and the Summer. Those with inhalant sensitivities, other than pollen, could be given concomitant study.

None of the patients, as far as could be discovered, suffered from food sensitivity.

All the patients chosen were receiving injection therapy for the pollens to which they were sensitive, and had been under treatment for three months or more before the vital capacity studies were done. None were told the reason for the studies, and none were asked regarding any sense of dyspnoea. The clinical histories were taken by physicians other than those who studied the vital capacity, and the data was submitted for mathematical analysis before any conclusions were drawn.

The vital capacity was taken with the patient in the erect position, the maximum expiration being measured, and the highest level of three trials being accepted. No children were included in the series, in order that the growth factor would not necessitate consideration. All of the patients had had x-ray studies to prove their lungs free from abnormality or infection. Since we were interested in the patient's changes in vital capacity relative to himself, we did not consider it as a degree of normality as determined by the patient's height, weight, age or sex.

The patients with ragweed pollenosis suffered an exposure to pollen longer than any of the others, and, giving as well the largest number of observations, were chosen for mathematical analysis. In order to have comparable data, two periods of time were chosen for all patients. The first period ran from May 25 to August 11, and the second period from August 12 to October 1. Although the

pollen slides for 1942 showed pollen to be present before August 11, this date had to be chosen because it was one of the days on which the Clinic was open. All of the patients had had sufficient observations of vital capacity in both periods to make the data comparable.

The variability in the observations was analyzed into variability between patients, between the periods, and the inter-action between the patients and the periods; that is, the variability due to different aspects of periods on different patients.

The inherent variability (that variability due to the differences of observations within the period patient block) was found by taking the sum of the squares about the patient block means. To make the comparison with the variability of means, the sum of the squares was divided by the harmonic mean of the number of observations in each block. The ratio of the variability due to the differences in period, and the inherent variability found in the above manner was 28.5. If there had been no effect due to the ragweed season, this ratio would not be expected to be greater than 6.78, more than once in a hundred times. The drop in lung capacity was, therefore, considered as highly significant.

The first table demonstrates the means by which the ratio of period sum of squares to inherent variability was obtained as $F = 28.5$.

Table 2 demonstrates in tabular form, the data used in the analyses of sixteen patients. All zeros have been omitted and the figures represent the vital capacity in units of 100 cc. (25 = 2500 cc.)

A third analysis was made in which the periods were studied. The mean sum of the squares between periods was found to be 13.9. This, as compared with the mean sum of the squares of the inherent variability of 2.43 showed a ratio of 53.8. This ratio is again comparable to the ratio of 6.78 described above, which should be expected only once in one hundred times.

An interesting observation not entirely pertinent to the subject matter of this paper was made. During the second week of May of the year in which the studies were done, there was a minor epidemic of colds observed both in private and public practice. No fewer than thirty of the forty-two patients reported severe upper respiratory infections during the first three weeks of that month. In all thirty, there was a significant drop in vital capacity during this period. The observations of the vital capacity diminutions before August 11 were taken as beginning on May 25, and do not take into consideration this abrupt fall due to intercurrent infection. Note will be made below of the similarity of the drop in vital capacity due to infection or compared to that caused by pulmonary involvement in pollen sensitivity.

It should be noted that the following charts do not present a continuous picture of the patient's vital capacity during the time in which he was under observation. We have no way of knowing what the vital capacity might have been between observations. A line drawn from one observation to the next, in chronological sequence, would imply that the vital capacity had progressively

TABLE 1

	First Period		*Second Period*		
Patient	n*	mean	n	mean	SUM
344392	12	27.500	3	26.333	53.833
136518	6	21.833	4	21.250	43.083
374920	2	28.500	4	24.750	53.250
404361	6	41.750	3	35.667	77.417
360415	7	24.214	4	24.250	48.464
404298	10	28.700	5	29.000	57.700
386375	21	24.667	7	24.857	49.524
407403	11	49.364	4	49.250	98.614
253719	9	27.289	6	27.167	54.456
407572	8	26.688	6	25.333	52.021
348491	10	35.900	3	35.500	71.400
376406	8	28.312	5	27.000	55.312
288351	5	19.200	2	19.500	38.700
408497	8	26.250	4	23.250	49.500
203996	9	25.333	3	23.667	49.000
407084	10	23.350	5	21.100	44.450
Sum		458.850		437.874	896.724

* n = number of observations.

Sum of squares of patient sums	53,592.248		
½ sum of squares of patient sums	26,796.124		
Correction term	25,128.560	° Free	Mean sq.
	1,667.564	15	111.171
Sum of squares of period sums	402,276,962		
1/16 sum of squares of period sums	25,142.310		
Correction term	25,128.560	° Free	Mean sq.
	13.750	1	13.750
Interaction	23.034	15	1.536

Sum of squares (corrected) for inherent variability	432.975	Harm. means of n's 1 / .198587	Mean sq. .483

$$**F = \frac{13.750}{.483} = 28.5$$

**F = ratio of period sum of squares to inherent variability.

TABLE 2

Data Used in Analysis
Ragweed Tests

Period 1: May 25 to August 11.
Period 2: August 12 to October 1.

PATIENT	Period 1	Period 2	PATIENT	Period 1	Period 2
344392	25	29	404298	30	28
	28	25		30	31
	27	25		28	31
	30			28	29
	31			29	26
	30			25	
	28			29	
	25			30	
	26			29	
	25			29	
	28				
	27		386375	24	24
				23	24
136518	21	21		28	25
	23	20		23.5	26
	22	22		23	25
	22	22		23	23
	21			23.5	27
	22			24	
				25	
374920	30	27		24	
	27	26		24	
		23		25	
		23		25	
				25	
404361	45	37		25	
	44	36		27	
	41.5	34		24	
	42			25	
	40			26	
	38			27	
				24	
360415	25	26			
	25	23.5	407403	50	50
	25	24		48.5	51
	22	23.5		47	50
	25			46	46
	24			50	
	23.5			50	
				50	
				50.5	
				50	
				49	
				52	

TABLE 2 (Continued)

Data Used in Analysis

PATIENT	Period 1	Period 2	PATIENT	Period 1	Period 2
253719	26	27	288351	17	20
	26.5	26		20	19
	26	28		20	
	27	27		20	
	27	28		19	
	29	27			
	28		408497	28	22
	29			28	27
	28			26	22
				27	22
407572	25	27		25	
	25	26		26	
	26.5	26		25	
	28	24		25	
	28	26			
	26	23	203996	24	25
	28			25	23
	27			26	23
				25	
348491	33.5	35.5		27	
	35	35.0		24	
	37	36.0		27	
	34			24	
	37				
	37		407084	21	21.5
	38			20.5	21.5
	36			27	19.5
	36			23	23.5
	35.5			25	19.5
				24	
376406	29	29		25.5	
	28	27		21.5	
	26.5	26		22	
	29	27		24	
	28	26			
	28				
	30				
	28				

increased or decreased during the interim period. The notations therefore should be viewed as disconnected phenomena related only by their chronological sequence, and not as representing curves of fluctuation. In all the profiles shown, the numbers represent 100 cc.—that is, 25. = 2500 cc. vital capacity.

P.N. (Plate 1): The vital capacity remained within the normal variation until early August, following which, it diminished during

all of the ragweed season, approaching its normal at the end of October. The patient reported little benefit as a result of his injection therapy. He had never before, and has not since, demonstrated any tendency toward bronchial asthma.

B.G. (Plate 2): The first drop in vital capacity occurs after August 12, reaching its nadir on September 8, the peak of the ragweed season, recovering slowly in late November. The patient reported little benefit from her injection therapy for her first season of treatment, with complete absence of symptoms in 1942, and a slight recurrence for 1943. No bronchial asthma.

A.N. (Plate 3): The pattern of the previous charts is reproduced with a rise of vital capacity approaching normal during a period in which there were three days of rain.

G.S. (Plate 4): The observations on the vital capacity are extremely erratic but nevertheless demonstrate a rise in vital capacity during a rainy period, and a fall in vital capacity coincident with the onset of symptoms unusually late during the ragweed season. The patient reported that her symptoms were late and mild in degree, and repeated a similar pattern in 1943 during which time she suffered for two weeks with typical allergic coryza. There has been no bronchial asthma.

Plates 5, 6 and 7 are included at this point for purposes of comparison. All three patients: N.G., S.C., and I.H., present typical clinical pictures of ragweed sensitivity causing allergic coryza and bronchial asthma and associated with equally well-marked dust sensitivity causing symptoms extra-seasonally.

It will be noted in comparison with the first plates shown that the observations demonstrate the vital capacity to be extremely

---

TABLE 3

Sum of squares about means in patient period blocks 432.975
Total observations minus number of means = 210 − 32 = 178
Mean sum of squares = 2.4324

Total for first period = 4099 Number of observations = 142
Total for second period = 1848 Number of observations = 68

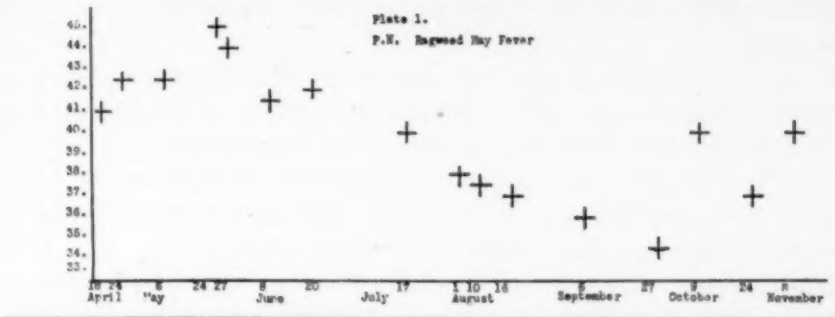
$$\frac{(4099)^2}{142} + \frac{(1848)^2}{68} = 168{,}544.6$$

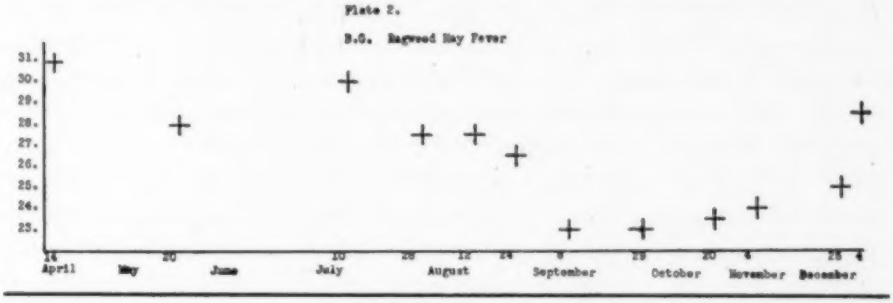
$$\text{Correction term} = \frac{168{,}414.4}{131.2}$$

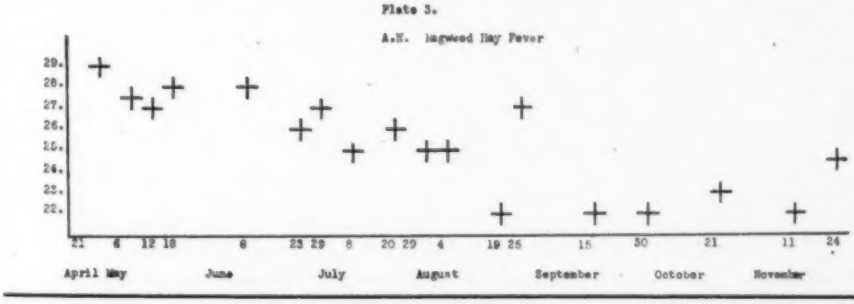
$$F = \frac{131.2}{2.4324} = 53.8$$

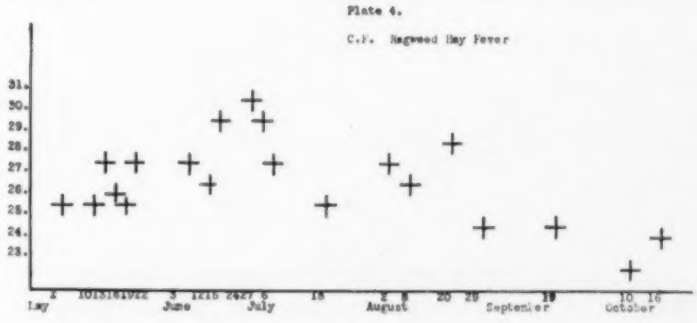
$F = 3.90$ is significant. $F = 6.78$ is very significant.

erratic with variations of 500 cc. or more. In all three patients however, the capacity of the lungs shows a marked fall during the ragweed season with a return to normal in the first two, during late October, and the third in late December. It should be noted that the observations presented in Plate 7 showed a gap from October 28 to January 6; and we do not know therefore, except









for the patient's clinical history, how soon after October 28 the capacity became that of her usual health, although she reports that her dyspnoea left her during the first week in November.

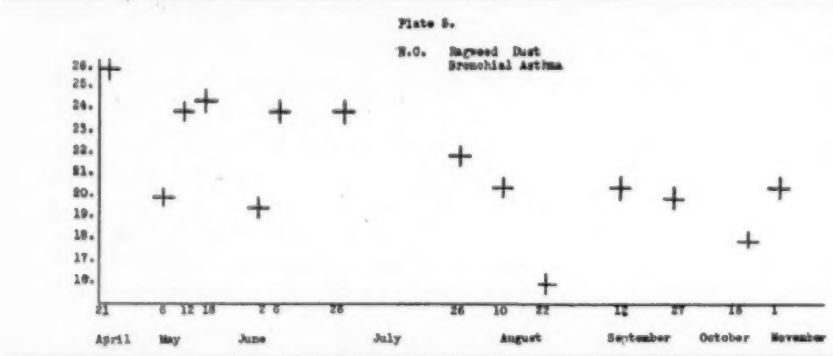
The Progress Notes for the patient who possessed vital capacity profile, as demonstrated in Plate 5, show that her hay fever has been reduced to a few sneezes each morning, and that her asthma is greatly improved and now only present with upper and lower tract infections; with nervousness, and with massive exposure to house dust.

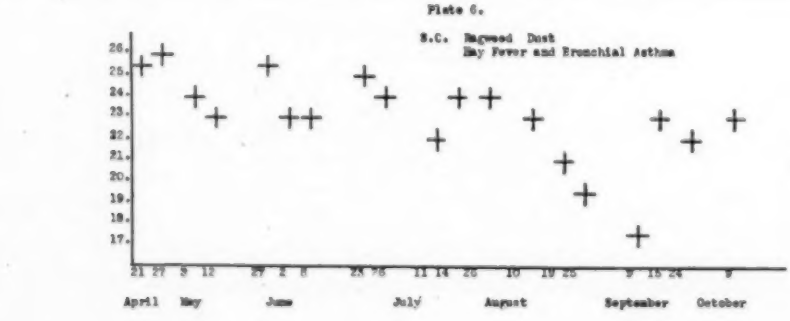
The patient whose studies are shown by Plate 6 reported some excellent results as far as her bronchial asthma is concerned, but states that her hay fever has shown little improvement.

I.H. (Plate 7), who presented marked severe symptoms in 1941, suffered from hay fever and bronchial asthma for eight weeks in 1942, and reported a fair result in 1943 and 1944.

In contrast to the above, A.L., whose vital capacity profile is shown in Plate 8, presented a typical ragweed and dust sensitivity associated with wheezing, perennial in type. There is a diminution of vital capacity during August and September, and extending to the end of October. The patient nevertheless reports excellent results with no symptoms excepting an occasional sneeze for the years of 1942 and 1943. There is no report for 1944.

C.S. (Plate 9), sequential sensitivities to timothy, ragweed, and sensitivity to dust caused an allergic coryza and occasional wheez-





ing. The vital capacity profile demonstrates a drop of vital capacity from 1900 cc. to 1100 cc. during the onset of the timothy season with a rise during the days in which there was a little pollen in the air due to climatic changes, and a further decrease at the peak of the grass pollen season during the first week in July. The pul-

Plate 7.

I.H. Ragweed Dust
Hay Fever and Bronchial Asthma

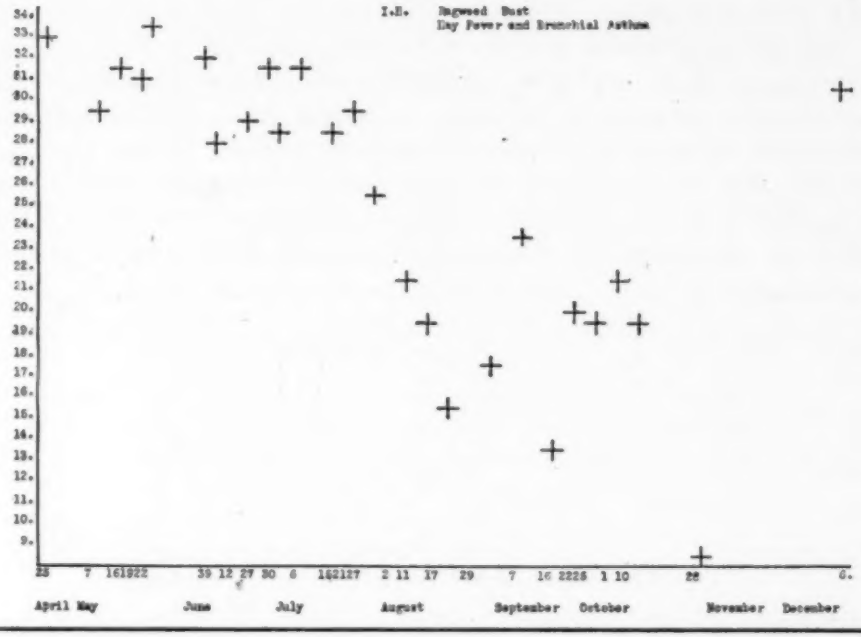


Plate 8.

A.L. Ragweed Hay Fever
& Bronchial Asthma

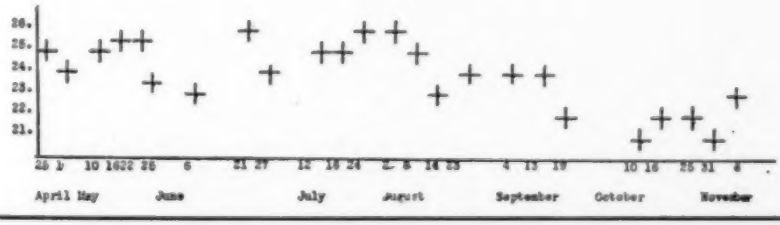
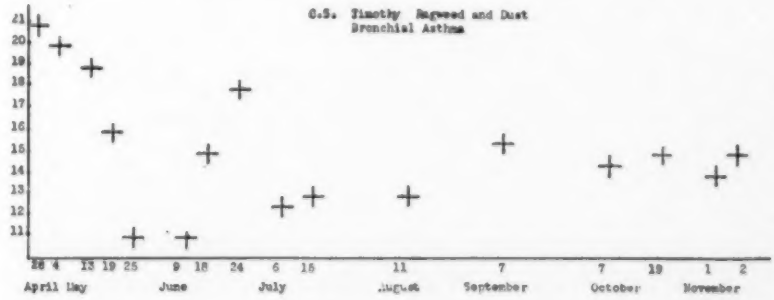


Plate 9.

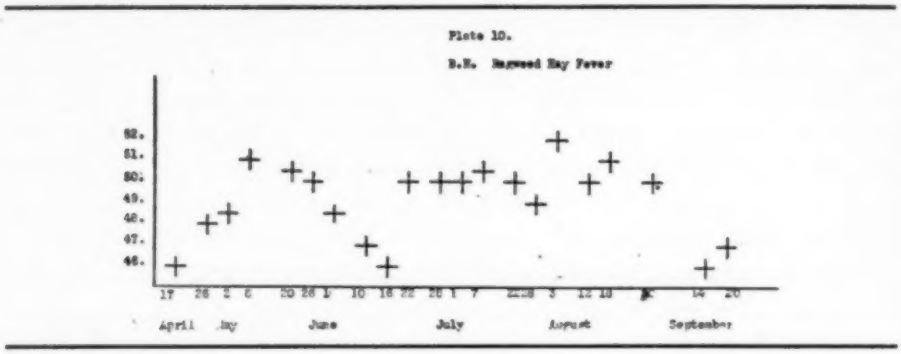
G.S. Timothy Ragweed and Dust
Bronchial Asthma

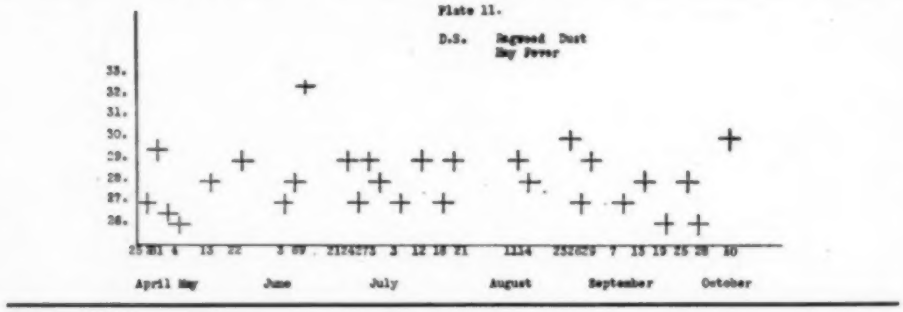


monary ventilation did not begin to approach normal until the first week in November.

B.H. (Plate 10), a patient with simple ragweed hay fever presents a profile interesting in the fact that although the vital capacity was at its lowest at the time of his maximum symptoms during the second week in September, he shows drops equal in altitude during mid-April when suffering from an infective coryza and in mid-June for no apparent cause.

The patients whose profiles were demonstrated in Plates 11 to 14 inclusive, D.S., A.E., B.F., and E.N., respectively, all demonstrate the typical profiles of patients suffering from dust sensitivity perennial in type, and pollen sensitivity limited to the ragweed season. The vital capacity in each case is extremely erratic and coincides with the patients' clinical symptoms, noteworthy only that the diminution of vital capacity occurs more frequently and





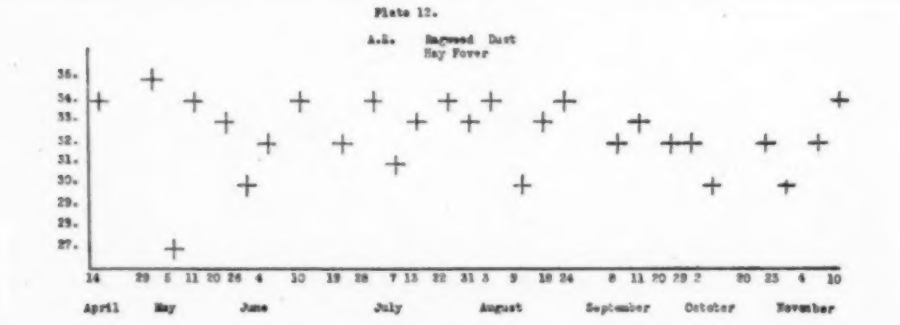


Plate 13.

B.F. Ragweed Dust
Hay Fever

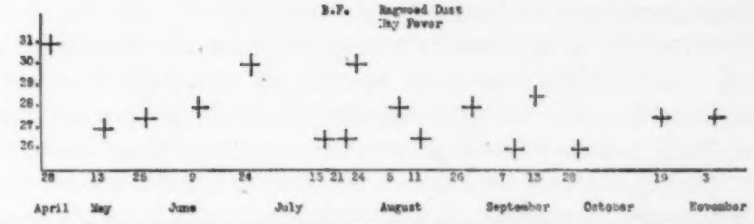


Plate 14.

E.H. Ragweed Hay Fever

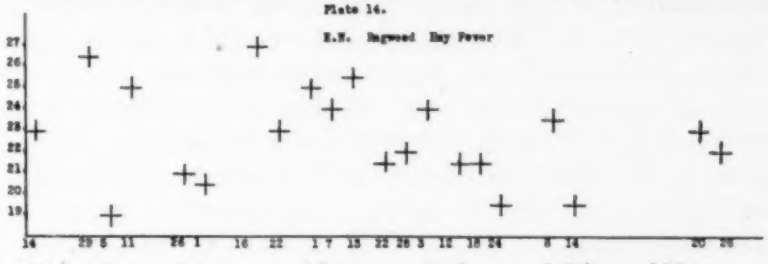


Plate 15.

C.C. Timothy Plantain
Ragweed Hay Fever and Bronchial Asthma

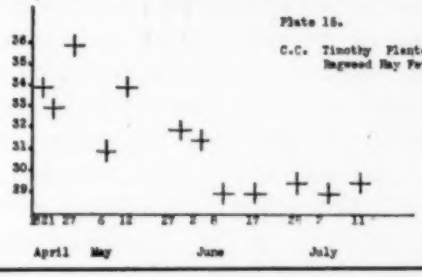


Plate 16.

S.W. Timothy Feathers Dust ? Ragweed
Hay Fever and Bronchial Asthma

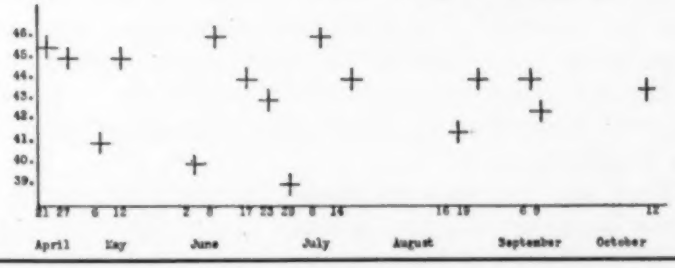
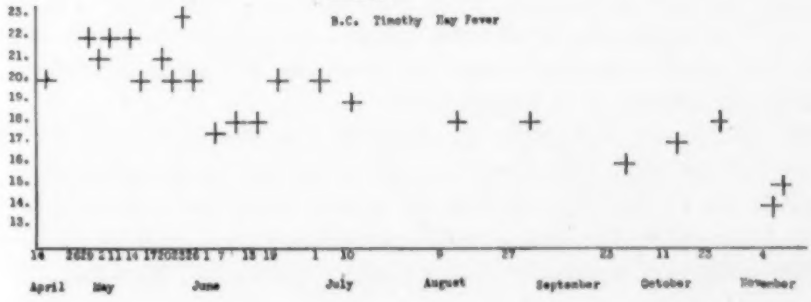


Plate 17.

B.C. Timothy Hay Fever



is slightly more marked during the period beginning August 12, returning to normal in November.

C.C. (Plate 15), a patient suffering from sensitivity to timothy, plantain and ragweed hay fever associated with bronchial asthma presented a decrease in vital capacity beginning during the last week in May, and becoming progressively less during the months of June and early July. There was no improvement as a result of treatment and the patient ceased attending the Clinic on July 11.

S.W., and B.C., as demonstrated in Plates 16 and 17 respectively, were sensitive to timothy; the first in addition to feathers and dust. Plate 17 showed the usual jagged irregular profile of the dust-sensitive patient with marked depression occurring during the first week in June and during the first week in July, coinciding with the first appearance of the timothy pollen and its maximum count. It will be noted that there is a depression in vital capacity during the first week in May, at which time there was an epidemic of colds, and again coinciding with the onset of the pollen season in August. During the year in which the patient was studied, he presented no ragweed pollen sensitivity although his skin test reaction to ragweed was positive. The subsequent history shows the following year he had severe ragweed sensitivity, and is now receiving treatment by injection with timothy pollen extract, ragweed pollen extract, and house dust extract. His sneezing and wheezing are still present although much diminished.

The patient delineated in Plate 17 has uncomplicated timothy sensitivity present for twenty years, with a gradual improvement leading to an excellent result. In 1944, she reported a perfect summer for a top dose of timothy pollen extract 12,000 P.N.U., excepting for a slight and probably insignificant diminution of vital capacity at the onset of the grass pollen season, and coincident with the onset of symptoms. She showed a fairly steady vital capacity presenting no diminution during the time that she was free of symptoms.

S.W. (Plate 16), has had treatment for six years for a number of inhalant sensitivities causing nasal and pulmonary symptoms. In 1942, he received injections of timothy pollen extract, feather extract, and house dust. In 1943, having previously given a positive skin test to ragweed, he showed clinical symptoms to weed pollen, and has since required injection therapy for exacerbations occurring in August and September.

B.F. (Plate 18), clinically sensitive to timothy and plantain with no history of bronchial involvement presents a depression in vital capacity in early May, during an upper respiratory infection; in early June when the grass pollen first appeared, and in late July at the time of the maximum plantain pollination. She had injec-

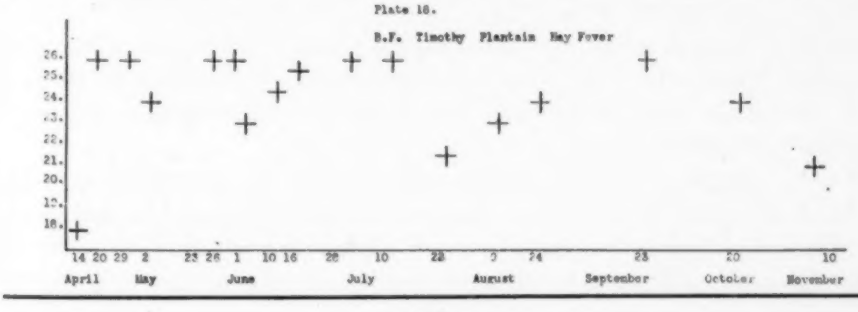
tion therapy from early 1940 until March 1942, and reports that in 1943 and 1944 she was completely free of all symptoms.

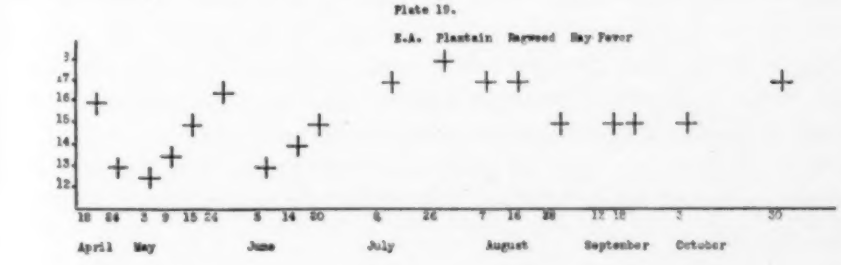
E.A., a patient with plantain and ragweed hay fever whose profile is shown in Plate 19 had an excellent result. In 1942, there were two bad days of symptoms during early June. There was the same amount of difficulty in 1943. The pulmonary capacity shows a decrease in vital capacity during the first week of June, and a slight decrease during the month of September.

The nineteen plates given are representative of those patients in whom vital capacity studies could be related to their sensitivities and their treatment. The remaining patients of the series showed similar profiles.

Of the forty-two patients studied, four are represented by profiles containing observations not sufficiently numerous to permit adequate interpretation. Twelve patients showed no correlation between the peaks and depressions of their vital capacity profiles as related to the dates of pollination of the plants to which they responded with nasal symptoms. None had bronchial asthma at the time the studies were done, and none has developed wheezing since. The excursion between the highest and lowest vital capacity readings is in all cases less than 300 cc. The remaining patients, twenty-eight in all, had a diminished vital capacity at the time of the onset or during the periods of maximum pollination of the plants toward which they demonstrated clinical sensitivity.

These patients studied during five pollen seasons show no apparent correlation between their diminished vital capacity and their prognosis. We may apparently conclude that among those





patients in whom there was a diminished vital capacity, the majority did not benefit greatly from their treatment. In the group of patients who showed no diminution in vital capacity, the majority received satisfactory benefit from their treatment.

In approximately one-third of the subjects in each group, there were patients whose vital capacity decreased, but who complained of no nasal or chest symptoms; just as there were those whose vital capacity remained level, but whose nasal symptoms were present in sufficient amount to cause complaint. As is to be expected, the patients who have an associated pollen asthma showed the greatest excursion in vital capacity measurement, especially marked in those who had additional sensitivities. In thirty of the forty-two patients, upper respiratory infections were associated with a significant drop in vital capacity.

SUMMARY

From these studies we may tentatively conclude that:

1. Patients with uncomplicated hay fever and no history of bronchial asthma may frequently demonstrate a diminished vital capacity during their pollen seasons.

2. In the majority of cases, such diminished vital capacity will be associated with little benefit from injection therapy.

3. The patients with coincidental inhalant sensitivities show greater variation in vital capacity measurement than those in whom there is a single causative agent.

4. Intercurrent nasal or pulmonary infection will also affect the vital capacity.

5. Patients with bronchial asthma due to pollen sensitivity, either alone or associated with other inhalant sensitivities, showed decreased vital capacity when exposed to their causative allergens, although clinically they may not complain of bronchial asthma.

6. In the small series studied, variation of vital capacity was not an index of prognosis.

7. The studies suggest that in three out of four patients the respiratory tract reacts as a single organ irrespective of the seat of the majority of the symptoms of which the patient complains.

8. Patients suffering from nasal pollenosis should be questioned regarding dyspnoea which may be the earliest sign of bronchial involvement. Studies with larger groups of patients, for longer periods of time, may finally prove how quickly this may be associated with a latent bronchial asthma in both treated and untreated pollen and other inhalant sensitive patients.

Similar studies are now in progress concerning the relationship of other forms of nasal allergy, and direct or reflex diminution in lung capacity.

RESUMEN

Basadas en estos estudios podemos sacar las siguientes tentativas de conclusiones:

1. Pacientes con fiebre de heno no complicada y sin antecedentes de asma bronquial demuestran frecuentemente disminución de la capacidad vital durante las estaciones de sus pólenes.

2. La mayoría de los casos con esta disminución de la capacidad vital obtienen poco beneficio con el tratamiento con inyecciones.

3. Los pacientes que tienen varias sensibilidades de inhalación revelan mayor variación de las mediciones de la capacidad vital que aquellos en los que existe un solo agente causativo.

4. Infecciones nasales o pulmonares intercurrentes también afectan la capacidad vital.

5. Pacientes con asma bronquial causada por sensibilidad a pólenes, sola o acompañada de otras sensibilidades de inhalación, mostraron disminución en la capacidad vital cuando se encontraban expuestos a los alergenos causativos, aunque es posible que clínicamente no se quejasen de asma bronquial.

6. En la pequeña serie estudiada, la variación en la capacidad vital no fue un índice del pronóstico.

7. Estos estudios indican que de cada cuatro pacientes, en tres las vías respiratorias reaccionan como si fueran un solo órgano, no importa cual sea la ubicación de la mayoría de los síntomas de los que se queja el paciente.

8. Pacientes que sufren de polinosis nasal deben ser interrogados acerca de disnea, la que puede ser el signo más temprano de complicación bronquial. Es posible que investigaciones de grupos más grandes de pacientes, por períodos de tiempo más prolongados, puedan comprobar finalmente la prontitud con que esta disnea puede estar asociada con asma bronquial latente en pacientes sensibles a pólenes o a otras inhalaciones, tanto tratados como no tratados.

Actualmente se están llevando a cabo estudios semejantes respecto de la relación entre otras formas de alergia nasal y la disminución directa o refleja en la capacidad pulmonar.

75 Bay State Road.

Roentgenographic Scanning of the Chest

SHERMAN W. ATWELL*
Boston, Massachusetts

Of all the roentgen examinations, that of the chest is best. Its position is the easiest; it seldom requires contrast media, it is by far the most productive in demonstration of abnormalities; and with the exception of bone films it offers the greatest detail. It has been such a tremendously important tool to medicine that there is a tendency to consider it infallible. However, in the comparison of surgically removed lungs with x-rays taken immediately before operation we find that roentgen examination is frequently fallible (Fig. 1). The flat plate by itself may record a coincidence of shadows which can assume a pathological pattern (Fig. 2), and even in the stereoscopic view, lesions may remain hidden or masquerade as normal or other misleading patterns (Fig. 3).

*c/o Richard H. Overholt, M.D., 1101 Beacon Street, Brookline, Mass.

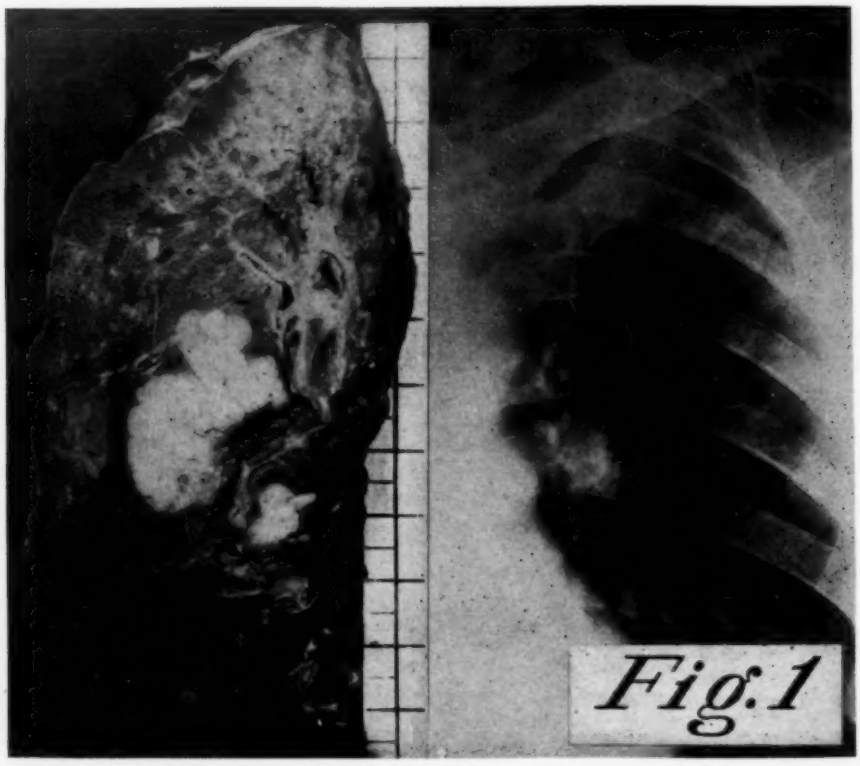


Fig. 1: A surgically removed lung and roentgenogram of the same lung taken the day before operation. The large dense tumor cannot be seen in the film.

The greatest reason for this fallibility is lack of scale in the x-ray emulsions and wave lengths of radiation which do not offer the maximum tissue differentation. The chest is composed of both very radiolucent and radiopaque areas. In exposing for the "thin" parts, the more dense areas are greatly underexposed, while exposure for the "heavy" parts badly overexposes the radiolucent portions. Consequently the most diagnostic films are those taken by a compromise exposure. The compensation factor of a radiolucent area equalizing a radiopaque part would not be found in stereoscopic films if there were greater scale to record them properly. It is unfortunate that the two parts needing the closest examination—the apex and the hilum—have the greatest tangles of black and white.

Since it is imperative for a thoracic surgical service to learn as much as possible about any abnormality, we have resorted to a comparison stereoscopic method to better evaluate pathology in extent and position.

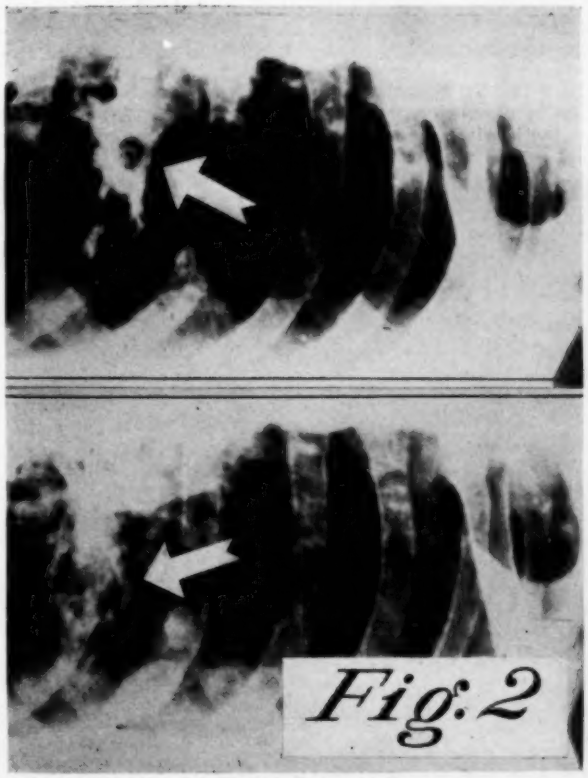


Fig. 2: Portions taken from each film of a stereo pair. Although the hilar region of each flat plate presents the appearance of abnormality, the lung was innocent by stereoscopic examination.

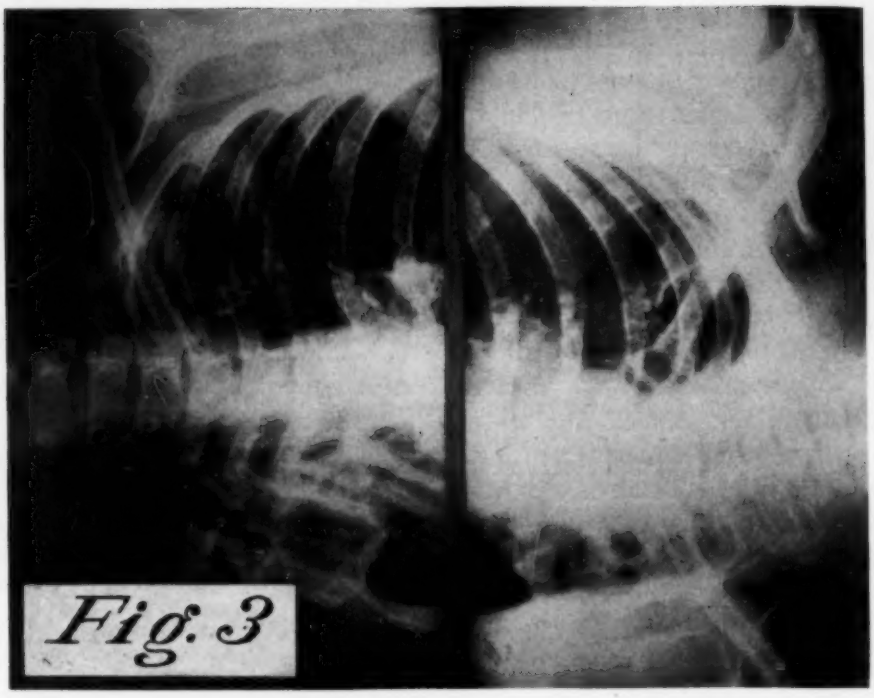


Fig. 3: One film from a scanning stereo of the apex of a referred patient. The right half clearly shows cavity in the unoperated side. Even stereoscopically the left half failed to demonstrate cavity.

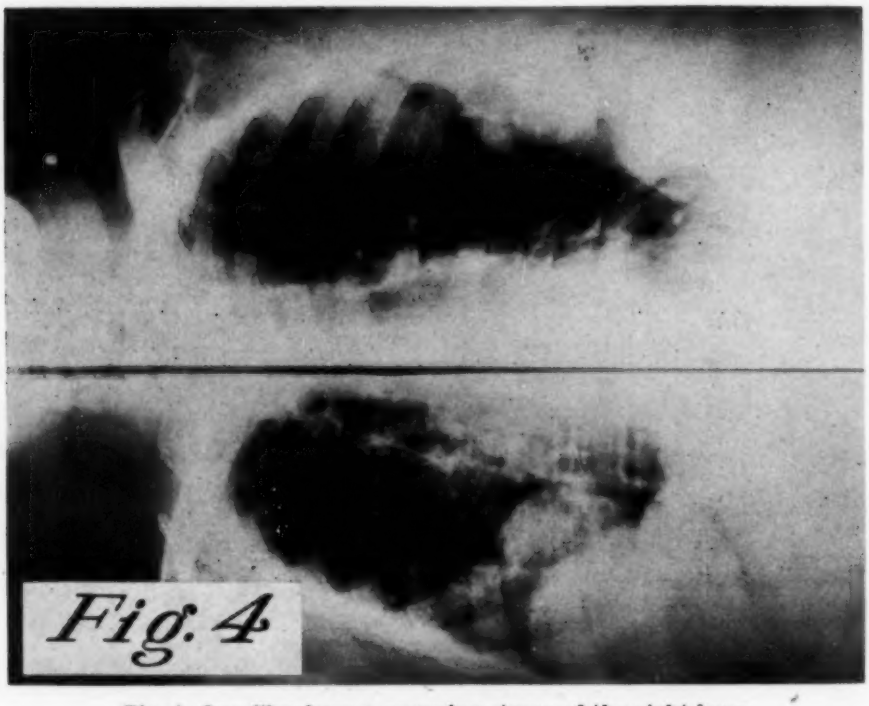


Fig. 4: One film from a scanning stereo of the right lung.

Considerations

Scanning, properly defined, is to "examine point by point". All binocular vision is, in a sense, scanning, but the conscientious artist, barber, pathologist, or surgeon will change his viewpoints in the close examination of an interesting area. Exercise of this ability should not be denied the roentgenologist. In viewing stereoroentgenograms, if comparison can be made only by changing the film sets, the lag in memory renders the comparison uncertain. Therefore, it has been valuable to make comparison stereos on the same set of films, to be viewed simultaneously. In this way the eyes are permitted frequently to wander back and forth, checking the different presenting shapes and positions of abnormalities against the relative anatomical landmarks.

The visual sense has been trained from infancy in evaluation of opaque matter. Probably primarily for this reason the interpretation of depth and shape in the transparent image is especially dependent upon peripheral borders. Consequently, it becomes of increased importance to have a comparison of these changed peripheral borders in order to gain a more comprehensive knowledge of any transparent or semi-transparent image.

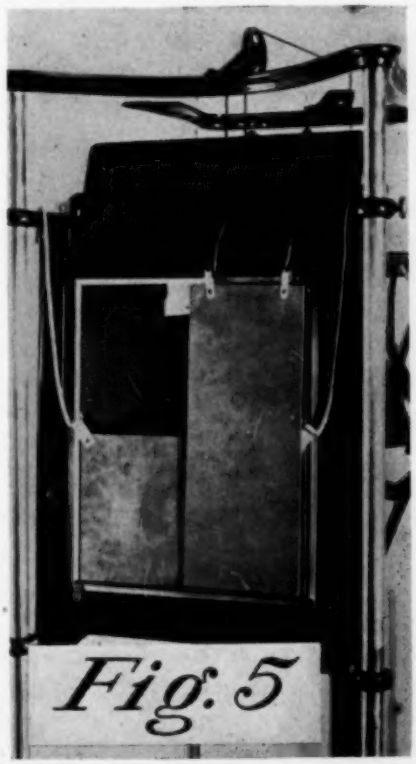


Fig. 5: Blocks and supports on the plate changer.

Stereoscopic scanning is indicated for those cases which still have doubtful areas after fluoroscopy and routine chest films have been seen. Comparisons can be made of the apex or of one entire lung. Angulation between the two positions comprising such a comparison examination should be sufficient to make visible the mediastinal portions of the lung, but not so great as to make comparison difficult. When the area is small or intricate, the angle between the patient-positions should be narrow. When the portion to be examined is large and gross, as in a large tumor or an extensive pneumothorax, the angle can be less acute.

Equipment

The only equipment needed is two pieces of lead or leaded rubber, one 17 x 7 inches, the other 14 x 8½ inches and improvised supports (Fig. 5). If a stereoscopic Bucky is not available, a Lysholm grid is frequently useful.

Procedure for Apex

Preparation for scanning stereos of the apex is simply done by blocking off the lower half of the front surface of the plate changer. The patient is placed in the postero-anterior position, then turned slightly into either anterior oblique position. Regular stereoscopic procedure is carried out. The cassettes are inverted and interchanged. The patient is then placed in the opposite anterior oblique position and stereo taken.

Procedure for Lung

The plate-changer is prepared by covering either long half with the 7 x 17 inch block. The patient is placed in the anterior oblique position and stereo taken. The block is then moved to the other side and the cassettes interchanged. The patient is then placed in the posterior oblique position and stereo taken. The interchange of cassettes renders this second image in the pseudoscopic position, making it more comparable with the first image (Fig. 4).

Variations and Combinations

If scanning stereos have been taken of a lung and abnormalities have been shown in only one view or shown so poorly in the complementary view as to be of no value, the area can be scanned in the preferable oblique position.

In especially intricate areas such as the sub-thoracoplasty lung, information frequently can be gained by using both blocks and taking four scanning views of the one questionable portion. In such a case it is often preferable to use a horizontal tube-shift.

In Figure 3, since the greater interest was in the unoperated

right side, right anterior and right posterior obliques were used. In this case, the cassettes were inverted but not interchanged.

CONCLUSIONS

1) The standard, flat roentgenogram of the chest can be inaccurate and misleading.

2) The single stereoroentgenogram of the chest is not always entirely comprehensive.

3) A comparison method of stereoscopically scanning an anatomical area may provide a check against error.

4) A comparison method of stereoscopically scanning an anatomical area can possibly demonstrate pathology not noted in another view.

5) The areas of pathology seen in both views will afford a comparison evaluation of extent, position, and shape.

CONCLUSIONES

1) El roentgenograma llano corriente del tórax puede ser inexacto y engañoso.

2) El estereoroentgenograma aislado del tórax no es siempre enteramente comprensivo.

3) Un método de comparación de escudriñar estereoscópicamente una zona anatómica, puede suministrar un control para evitar el error.

4) Un método de comparación de escudriñar estereoscópicamente una zona anatómica posiblemente puede demostrar procesos patológicos que no se notan en otra proyección.

5) Las zonas patológicas que se observan en ambas proyecciones permiten una apreciación comparada de la extensión, posición y forma.

Iodized Oil in the Treatment of Chronic Bronchitis

FRANK T. HARPER, M.D.
Burlington, North Carolina

In the last 25 years our knowledge of respiratory diseases has increased considerably, especially in the matter of more accurate diagnosis. Due to improvement in thoracic surgery, and the advent of the sulfonomides and penicillin, much advance has been made in the treatment of some of those diseases. There still remains chronic bronchitis, which eludes both surgery and chemotherapy.

Chronic bronchitis is an inflammation of the bronchial tubes, and is usually caused by some pre-existing upper respiratory condition interfering with the circulation or drainage of the bronchial tract and is usually diagnosed under a dozen or more pathologic appelations. The symptoms are cough, with or without expectoration, accompanied by mild or severe constitutional symptoms. Coarse scattered rales are the usual rule. The etiology of bronchitis is too numerous for discussion here, ranging from infection to foreign body and allergy. Of the latter, I can say it plays an all important role in chronic cough and a complete allergic study should be made of all cases. Bronchoscopy should be done also to rule out foreign body and neoplasms.

The multiplicity of remedies brings to mind the fact that none are particularly good. In review, various results have been reported with x-ray therapy,[1] thiamine chloride,[2] vaccines, arsphenamine, poultices, Dover's powders, cough sedatives, expectorants,[3] bronchial instillations, inhalants, sulfonomides, and recently by respiratory exercises.[4] Worthy of special mention are the so-called "expectorants". Alstead,[5] after much work reported "there is no evidence that either ammonium carbonate or ammonium chloride has any effect on expectoration in bronchitis". He reached similar conclusions on potassium iodide and ipecacuanha. Furthermore, he feels as if "this is one department of therapeutics that has registered no improvement in the last half century". My results with these expectorants have been very unsuccessful. To add with this group paregoric[6] made its bow. Warning should be made also of the widespread use of narcotics in cough sedatives. I have seen prescriptions using ¼ grain of morphine and some with 1/20 grain of dilaudid to the dose. The dangers of this are perfectly obvious.

Two Frenchmen, Sicard and Forestier,[7] in 1922 pioneered the

use of iodized oil as a diagnostic procedure for bronchiectasis and in addition found clinical improvement! Since then relatively few papers have been presented.[8,9,10,11,12,13,14]

The chief indication for the use of iodized oil is chronic cough, with or without expectoration, in non-tuberculous patients who have not responded to the usual forms of treatment. The contra-indications are 1) active pulmonary tuberculosis, 2) acute infection, 3) myocarditis, especially with pulmonary edema, 4) patients sensitive to iodine.

The oil I used is iodochlorol (Searle), which contains 27.0 per cent iodine and 7.5 per cent chlorine in organic combination with highly refined oil. There are various methods of instilling oil, which have been adequately described by Oschner,[15] J. J. Singer,[16] Prichard,[17] Rosenthal,[18] and Davenport and Adams.[19] After instillation, the oil is partly expelled by cough and that which goes into the finer bronchi and alveoli remains in situ and is generally absorbed. Some is taken to lymph nodes by phagocytes. The iodine

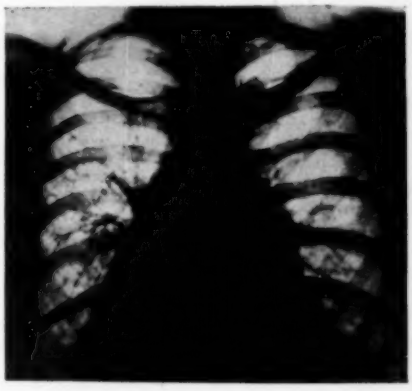


Fig. I: M.C. — W.F.M. — 23

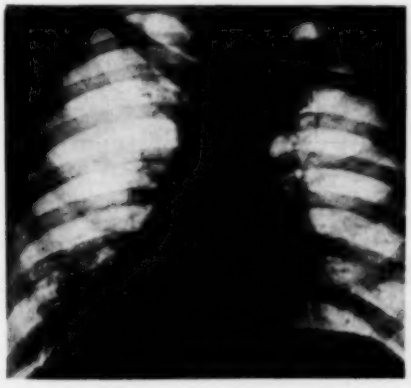


Fig. II: D.P. — W.M.M. — 38

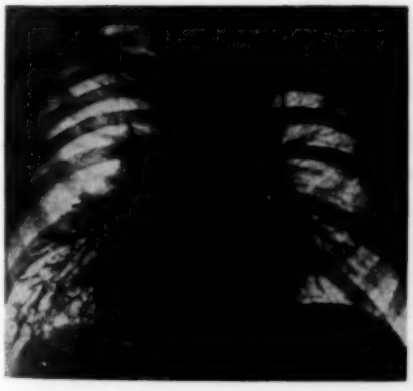


Fig. III: O.A. — W.M.M. — 28

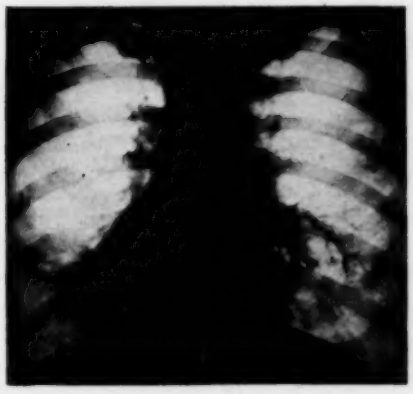


Fig. IV: J.H.L. — W.M.F. — 44

is secreted in urine, saliva, and sweat. X-ray studies show that there is a retention in the lungs from 24 hours to two years.

The accompanying chart shows the results we have obtained in treating 43 patients.

Total	M	F	Co-Existing Conditions							
			Asthma	Inactive tbc.	Hemoptysis	Hypertension	Bronchiectasis	Menopausal	Psychosis	Epilepsy
43	18	26	4	1	7	1	6	1	1	1

Results

Good		Moderate		Poor	
No.	Pct.	No.	Pct.	No.	Pct.
28	65.8%	11	26.3%	4	7.9%

SUMMARY

I have used iodized oil in the treatment of 43 patients for chronic bronchiectasis. Eighteen of these were males and 26 were females, the ages ranging from 7 to 65 years and the complications consisting largely of hemoptysis, asthma, inactive tuberculosis, hypertension, bronchiectasis, menopausal, psychosis and epilepsy. The results were good in 28 cases, moderately good in 11 cases and poor in 4 cases. In the majority, results were obtained after one instillation, but it has been necessary to repeat 11 of these, at their request.

RESUMEN

He usado aceite yodado en el tratamiento de 43 enfermos con bronquitis crónica. Dieciocho de ellos varones y 25 mujeres, sus edades variaban de 7 a 65 años y las complicaciones, en su mayor parte, consistieron de hemoptisis, asma, tuberculosis inactiva, hipertensión arterial, bronquiectasia, sicosis de la menopausia y epilepsia. Se obtuvo buenos resultados en 28 casos, moderadamente buenos en 11 casos y malos en 4 casos. En la mayoría se obtuvo resultados después de una sola instilación, pero fue necesario repetir 11 instilaciones a solicitud de los enfermos.

REFERENCES

1 Bond, R. C., and Clovis, C. H.: "X-Ray Therapy in Bronchitis in Children," *W. Virigina M. J.*, 32: 345, 1936.
2 Morehead, O. J.: "Vitamin B_1 in Chronic Bronchitis," *Northwest Med.*, 40: 212, 1941.
3 Holmes, C. H.: "Acute Bronchitis," *J.M.A., Georgia*, 30: 60, 1941.
4 Taylor, A. B.: "Chronic Pulmonary Catarrh in Childhood," *Brit. M. J.*, 1: 453, 1944.
5 Alstead, S.: "Potassium Iodide and Ipecacuanha as Expectorants," *Lancet*, 2: 932, 1939.
6 Boyd, E. M., and MacLachlan, M. L.: "Expectorant Action of Paregoric," *Digest of Treatment*, 8: 164, (Sept.) 1944. (From Canad. M. A. J., 50: 338, 1944).
7 Sicard, J. A., and Forestier, J.: "Iodized Oil as Contrast Medium in Radioscopy," *Bull. et mém. Soc. Méd. d. hop. de Par.*, 46: 463, 1922.
8 Tewksberry, W. D., and Fenton, E. R.: "Therapeutic Use of Iodized Oil in Chronic Bronchitis and Bronchiectasis," *M. Ann. District Columbia*, 8: 227, 1939.
9 Cole, D. B., and Nalls, W. L.: "Twelve Years' Experience with Iodized Oil," *Virginia M. Monthly*, 65: 336, 1938.
10 Blumberg, N.: "Bronchiectasis, with Description of Perinasal Method of Introduction of Iodized Oil for Diagnosis and Treatment," *Dis. of Chest*, 3: 15, 1937.
11 Burge, F. W., and Post, J. W.: "Lipiodol Bronchography," *Dis. of Chest*, 4: 20, 1938.
12 Balyeat, R. M.: "Therapeutic Value of Iodized Oil Intratracheally in Bronchitis," *Southwestern Med.*, 21: 341, 1937.
13 Alison, J. F.: "Asthmatic Bronchitis: Treatment with Iodized Oil (Lipiodol)," *South. M. J.*, 26: 696, 1933.
14 Taylor, J. H.: "Treatment of Asthmatic Bronchitis with Iodized Oil," *Minnesota Med.*, 15: 408, 1932.
Fink, L. W.: "Lipiodol as a Therapeutic Agent in Asthma," *Minnesota Med.*, 15: 522, 1932.
15 Ochsner, A.: "Use of Iodized Oil in Treatment of Bronchiectasis," *S. Clinic North America*, 10: 843, 1930.
16 Singer, J. J.: "A Simple Method of Introducing Iipiodol into the Lungs," *Tr. Am. Laryng., Rhin. and Otol. Soc.*, 448, 1927.
17 Pritchard, S.: "Use of Iodized Oil in Diagnosis and Treatment of Bronchial Affections," *Southwestern Med.*, 11: 448, 1927.
18 Rosenthal, G.: "Technic for Intercricothyroid Injections," *Paris Méd.*, 10: 521, 1920.
19 Adams, R., and Davenport, L. F.: "Technic of Bronchography and System of Bronchial Nomenclature," *J.A.M.A.*, 118: 111, 1942.

Pulmonary Disease Secondary to Cardiospasm, with Acid Fast Bacilli in the Sputum
(Case Report)

EMIL ROTHSTEIN, M.D.,* *and* H. B. PIRKLE, M.D., F.C.C.P.**
Rockville, Indiana

A well recognized cause of pulmonary disease is aspiration of foreign bodies. Cardiospasm is a condition predisposing to aspiration, as it produces in close proximity to the larynx a dilated esophagus containing large amounts of foreign material; in addition this foreign material is present at night, when the reflexes are dulled. Nevertheless, aspiration sufficient to cause disease is apparently rare. A search through a number of standard textbooks of medicine[1-7] reveals no mention of this condition. Two cases of pulmonary disease associated with cardiospasm but without acid fast bacilli in the sputum have been reported recently. Sampson's[11] case was a lung abscess localized in the lower portion of the right lung and Schrire's[12] case was one of bilateral bronchiectasis. Dr. Amberson[13] in discussing Sampson's case indicates that pulmonary disease under such circumstances is not extremely rare and is characterized by abscess formation or by a mild organizing or suppurative pneumonia. However, it is clear that the medical profession is not familiar with this condition, as indicated by the textbooks of medicine quoted above.

CASE REPORT

T. M., a white woman of 31 was admitted to the Indiana State Sanatorium May 17, 1943, with a diagnosis of bilateral tuberculous pneumonia. This illness began April 10, 1943 with "double pneumonia" characterized by chest pain, and fever to 103°; this was soon followed by cough, sputum, chilliness, night sweats, anorexia, weakness, weight loss, etc. These symptoms continued to her admission, her temperature going to 102-103° daily. During the week preceding her admission she felt slightly better. She had been treated with much "sulfa" medication by mouth and rectally, with no definite benefit. Her sputum examined before admission on one occasion showed 6 acid-fast bacilli.

Examination showed her to be acutely ill, dehydrated and hypotensive. There were many fine and coarse rales throughout, chiefly in the lower half on each side.

The white count was 14,250, with 90 per cent polymorphonuclears; red count, 4.9 million; sedimentation index, 16 mm. in one hour.

---

*Assistant Medical Director, Indiana State Sanatorium.
**Acting Superintendent and Medical Director, Indiana State Sanatorium.

Sputa were repeatedly negative for acid fast bacilli on direct examination: During the first three weeks of her stay, two 24-hour, three 48-hour, and two 72-hour sputa were examined by the concentration method. Three of these were cultured and were found to contain acid fast bacilli.

X-ray (Fig. 1), May 17, 1943: Right: Coarsely mottled conglomerate infiltration with multiple cavitation in upper one-half; moderately coarsely mottled infiltration in the lower one-half. Left: Conglomerate coarse infiltration with multiple small cavitation in the central lung field. This was diagnosed as pulmonary tuberculosis, far advanced, bilateral with cavitation, and a poor prognosis was given.

Subsequent course: When 7 consecutive sputa were negative in spite of profuse purulent expectoration, an attempt was made to reconsider the diagnosis. By this time the patient was free of fever and on detailed questioning gave the information that for a number of years she had vomited very easily. Food seemed to stick substernally and would cause some choking upon swallowing. This was more pronounced with liquids than with solids. Regurgitation would sometimes occur upon lying down. This led to a tentative diagnosis of cardiospasm; Belladenal-Sandoz (containing phenobarbital and belladonna) was prescribed, two tablets every four hours at first and later four tablets daily, with marked relief of the gastro-esophageal symptoms. When her condition permitted, an esophagram was made revealing (Fig. 2) marked esophagectasis secondary to cardiospasm (achalasia of the cardia). During the months of her stay, her chest x-rays showed gradual improvement (Fig. 3). All her x-rays reveal a mediastinal shadow widened to the right; on the original films a fluid level can be seen at the fifth posterior rib but this is not visible on the illustrations. This latter was not noted until the esophagram had been made; hindsight then revealed it.

During her stay, 14 sputa were examined by concentration methods; of these, 8 were 72-hour specimens: all were negative. Cultures revealed acid fast bacilli on sputum raised in May and June, 1943 and were negative on 5 subsequent occasions.

Tuberculin testing with PPD gave a negative reaction to the first strength and a positive to the second strength. Through the courtesy of Dr. Edward R. Baldwin of Saranac Lake, we tested this patient with "P" tuberculin, made from the case reported by him.[9] She had a 48 hour positive reaction with .1 and 1 mgm., consisting of areas of redness, induration and soreness of 2.5 cm. and 3.5 cm. respectively. It will be recalled that her tuberculin test with first strength PPD was negative although the second strength gave a well marked reaction. The "P" tuberculin was tried on ten individuals, 8 being tuberculous. The results were as follows with .1 mgm.; 24 hours: 8 showed positive reactions, about 1 cm.; 48 hours: all were now negative but one; the reaction here was 1 cm. in diameter. We interpret these reactions as indicating that our patient was sensitive to the "P" tuberculin, and more so than any of ten individuals selected at random. Considering the extent of her pulmonary lesion, the reaction to "P" tuberculin and lack of reaction to first strength PPD must be regarded as strongly supporting a diagnosis of non-tuberculous pulmonary disease. She gained 30 pounds, became symptom free (while taking Belladenal) and was discharged for dilatation treatments.

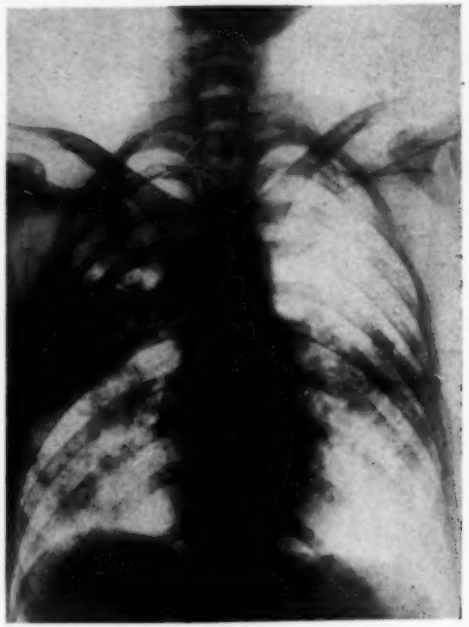


FIGURE 1

FIGURE 2

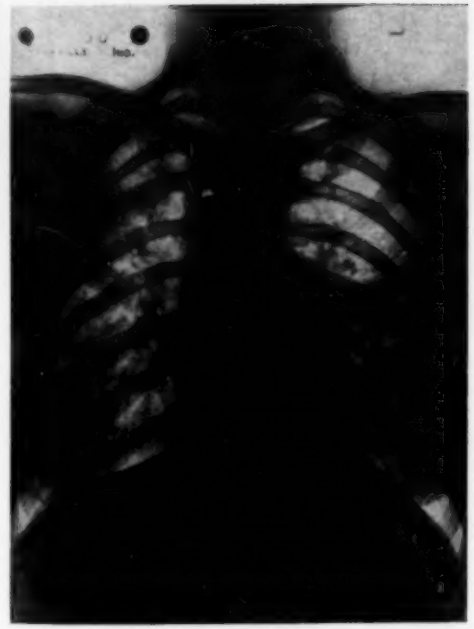


FIGURE 3

Fig. 1: May 17, 1943: Reveals patchy consolidation of the right upper lobe with suggestive cavitation. Moderately coarsely mottled infiltration in the right lower lung field and in the left central lung field. Widening of the upper mediastinal shadow to the right.

Fig. 2: Sept. 16, 1943: Reveals marked dilatation of the esophagus with cardiospasm, the dilated portion projecting slightly into the right lung field.

Fig. 3: July 17, 1944: Reveals marked clearing, right and left with some residual fibrosis and infiltration throughout the right lung and in the central portion of the left lung. There is uniformly increased density in the right upper mediastinal region terminating at the level of the 4th posterior rib.

Discussion

The chief point requiring clarification in this case is the finding of acid fast bacilli on four occasions at the onset of the illness. Warring and Rilance[8] encountered a similar case—the x-ray being a "dead-ringer" for ours. They cultured the organism and found it to be a nonpathogenic (for guinea pigs) saprophyte which grew out well in 24 to 48 hours and which changed on subcultures to acid fast coccoid bodies with some fine, faintly staining filamentous forms. They made a "tuberculin" of this organism to which their patient was highly sensitive but which gave no reaction or a very slightly positive reaction in other, tuberculin positive patients. Baldwin[9] also reported a similar case (the x-ray also resembling ours quite closely) where the sputum was always raised by vomiting. An acid fast saprophyte, nonpathogenic for laboratory animals, was isolated. A "tuberculin" made from this organism was found to give a markedly positive reaction, as did one made from timothy hay bacilli; the reactions to these were greater than those to true tuberculin. Unfortunately the positive cultures in our case were discarded before the non-tuberculous nature of the disease was realized and the cultures were subsequently negative. Skin tests were positive with Dr. Baldwin's "P" tuberculin, as described above.

It is our belief that this patient does not have tuberculosis. The following points are the reasons for this belief: 1) On admission she had profuse expectoration, purulent in nature, and this persisted for a number of months. In spite of this fact no tubercle bacilli were found on direct smear, although during the first few weeks all the sputum raised over a period of 14 days was examined by the concentration technique. 2) Her rapid clinical recovery and x-ray improvement in spite of her extremely poor condition on admission and the very extensive amount of disease as seen on the x-ray, apparently with bilateral cavitation. 3) The early disappearance of the acid fast bacilli from the sputum as studied on culture. 4) The marked resemblance between the x-ray in our case and x-rays of the other cases[8,9] reported of the same condition. 5) The results of skin testing with "P" tuberculin.

Although cardiospasm is a common condition it is apparent that pulmonary disease associated with it is very infrequent. The presence of acid fast bacilli in the sputum in such a case has only been reported in three previous cases.[8,9,10]

The similarity of the x-rays in two other cases[8,9] with our own tempts one to construct a syndrome which can be recognized roentgenologically—bilateral upper lobe dense infiltrations with highlights, associated with widening to the right of the mediastinal

shadow. The pulmonary lesion is found chiefly at the bases of the upper lobes, and so reaches down farther on the left. Coarse infiltration may be present in the lower lung fields. We realize that three cases may well constitute a coincidence rather than a syndrome and therefore await with interest further cases of the same sort.

One should also realize that not all acid fast bacilli are tubercle bacilli; this is especially true when the organisms are found on gastric examinations. Baldwin found acid fast bacilli on the surfaces of various fruits and vegetables and these resembled the timothy hay bacilli (B phlei). These might be present occasionally between the teeth or in the stomach contents and give a false culture.

SUMMARY

A case of acute pneumonitis, becoming a chronic fibrosing process, is described in a patient with esophagectasis secondary to cardiospasm (achalasia of the cardia). A few acid fast bacilli were found in the sputum during the early months of the illness. The x-ray presented certain features which may enable this condition to be recognized roentgenologically as well as clinically.

RESUMEN

Se describe un caso de neumonitis aguda, que se convirtió en un proceso fibroso crónico, en un enfermo con esofagectasia secundaria a cardioespasmo (falta de dilatación del cardias). Se encontraron unos pocos bacilos ácidoresistentes en el esputo durante los primeros meses de la enfermedad. La radiografía presentó ciertos rasgos que pueden permitir que se diagnostique este estado tanto radiográficamente como clínicamente.

REFERENCES

1 Blumer: "Besside Diagnosis," *Saunders,* 1929.

2 Cecil: "Textbook of Medicine," *Saunders,* 6th Edition, 1943.

3 Meakins: "Practice of Medicine," *Mosby,* 1936.

4 Musser: "Internal Medicine," *Lea & Febiger,* 1938.

5 Nelson: "Looseleaf Living Medicine."

6 Price: "Textbook of the Practice of Medicine," *Oxford,* 5th Edition, 1937.

7 Tidy: "Synopsis of Medicine," *Wood,* 7th Edition, 1939.

8 Warring, F. C. Jr., and Rilance, A. B.: "Chronic Indurative Pneumonia Resulting from Cardiospasm; Case with Nonpathogenic Acid-Fast Bacilli in Sputum," *J. Lab. & Clin. Med.,* 28: 1591, (Oct.) 1943.

9 Baldwin, E. R.: "Nonpathogenic Acid-Fast Bacilli; Case of Chronic Pneumonitis Associated with Nonpathogenic Acid-Fast Bacillus; Presence of Acid-Fast Soil Bacteria on Raw Fruits and Vegetables," *Am. Rev. Tuberc.,* 45: 756, 1942.

10 Cummins, S. L., and Williams, E. M.: " 'Acid-Fast' other than Koch's Bacillus Cultivated from Sputum," *Tubercle,* 15: 49, (Nov.) 1933.

11 Sampson, D. A.: "Lung Abscess due to Esophageal Overflow," *New England J. Med.,* 219: 982, (Dec. 22) 1938.

12 Schrire, T.: "Bilateral Bronchiectasis with Cardiospasm," *Lancet,* 2: 1225, 1938.

13 Amberson, J. Burns: "Yearbook of Gen. Med.," *Yearbook Publishers,* p. 260, 1939.

Bulla of the Lung

E. ROBERT WIESE, M.D.*
South Mountain, Pennsylvania

Bulla of the lung is a pathological entity caused by the confluence of two or more of the terminal elements of the bronchial tree. The condition is usually associated with vesicular emphysema at any age and probably exists more frequently than is suspected in cases of tuberculosis, anthracosilicosis and other conditions where emphysema is often present to greater or lesser degree. Bullae may be found subsequent to any condition that interferes with normal respiratory mechanism such as lung tumors, mediastinal new growths, localized scar tissue or oedema of the bronchus, areas of atelectasis or consolidation and heavy tenacious mucus within the bronchus. Benjamin and Childe[1] have reported an interesting series of cases associated with pneumonia in children.

A single bulla is probably a rarity; they are usually multiple in number and occupy portions of the lung most moveable and least subject to continuous pressure of the chest wall, hence are most frequently found in the upper anterior as well as along the mediastinal aspects of the lung. They may vary in size from that of a small vesicle to that of a large grape fruit.[2,3]

Bullae are formed by any acute—but more often, chronic intra-alveolar pressure sufficiently great to stretch and eventually destroy the inter-alveolar walls. According to von Hansemann[4] normal alveoli communicate with each other by means of minute perforations in the inter-alveolar walls, although the existence of these in normal tissue is disputed by other authorities.

There are two views as to the formation of bullae of the lung. The advocates of the first of these contend that should there arise within or without the bronchus or bronchi a condition which diminishes the lumen of these passages the normal respiratory mechanism is disturbed and the intra-alveolar pressure will be increased as the expiratory force is less than the inspiratory force. They contend that these minute perforations (Kohns pores) in the inter-alveolar walls become larger and larger until finally there remain between the adjacent alveoli only a few strands, made up for the most part of elastic tissue and blood vessels.[5] Finally these also disappear and there is thus formed a bulla whose size depends upon the number of alveoli that have become confluent.

---

*Mont Alto Sanatorium.

The advocates of the second view believe that the inter-alveolar walls are destroyed by atrophy due to excessive stretching subsequent to the increased intra-alveolar pressure. The process extends from alveoli to alveoli, from acinus to acinus until even the better part of an entire lobe may be involved. Naturally anything that tends to increase the intra-alveolar pressure, such as severe coughing attacks, dyspnoea, etc., will hasten the destruction of the inter-alveolar walls.

The distinction between bullae and blebs should be borne in mind as the two terms are not synonomous despite the loose use of the words by some writers. Bullae are formed in the lungs of patients afflicted with vesicular emphysema; blebs are present in cases of interstitial emphysema. A bleb is formed by the rupture of the alveolar wall; the air escaping through the tear separates the pleura from the alveolar wall lying underneath it, much like a dissecting aneurysm. Bullae are always definitely a part of the lung tissue and are in direct connection with a bronchus; blebs, on the contrary, are movable under the pleura and have no direct bronchial connection. At autopsy bullae of any appreciable size bulge from the surface of the lung, blebs, however, collapse when there is no longer any influx of air and the pleural space is opened.

Bullae of the lung are by no means innocuous. The danger of rupture of the thin pleural wall while not usual is by no means rare, and there are several reports where fatal spontaneous pneumothorax was directly referable to such a mishap.[6,7,8,9]

There is no clinical sign or symptom characteristic of bullae of the lung. Associated as it most often is with vesicular emphysema one generally finds present the signs and symptoms of that condition, i.e., rapid and shallow breathing, barrel-shaped chest, elevated clavicles, shortened neck, rounded shoulders, increased anterior-posterior diameter of the chest, horizontal position of the ribs, depressed diaphragm, poor chest expansion, loss of cardiac and often hepatic dullness, feeble breath sounds with prolonged expiration, cough and sputum.[10] Should the bullae attain any appreciable size, dyspnoea and cyanosis become quite marked and there is reduction in the total vital capacity.

In the presence of pulmonary tuberculosis, tumors of the lung, anthracosilicosis, etc., the signs and symptoms of any emphysema that is present are overshadowed by the principal disease. When in such cases the pulmonary involvement seems inadequate to account for the pronounced shortness of breath and cyanosis that may be present the presence of bullae should always be suspected.

The diagnosis, when made during the life of the patient, is nearly always reached by means of the roentgenogram where bullae may be recognized as localized areas of rarefaction in the lung fields

surrounded invariably by a thin and sharply defined border. This hairline is in sharp contra-distinction to the heavy outlines seen as a rule in cavitation due to pulmonary tuberculosis, abscess, etc. Bulla may readily be mistaken for spontaneous pneumothorax, but in case of pneumothorax one can generally trace the line, indicative of the lung surface, to the mesial side of the air space; this line, usually denser than the hairline seen in bulla, courses toward the base of the lung in the majority of cases, whereas in bulla the line curves upward from a well defined curved base of the air space either to merge with the pleural shadow in the axillary line or to form an oval, spheroid, or even lobulated well illuminated space. In some instances it is possible to discern the remnants of some of the alveolar walls, especially when viewed stereoscoptically. It may be said here that it is not unlikely that the so-called "ring shadow or annular rings" formerly discussed may have been due to bulla formation. Freedman[11] claims that Laurell[12] was the first to establish that fact.

It will be apparent that bullae must have reached an appreciable size before diagnosis is possible roentgenologically.

The presence of fluid in a cavity of doubtful origin is of no diagnostic value as such may occur in bullae; when fluid does accumulate in a bullae it is likely to become infected quite readily because of the direct communication of the bulla with a bronchus.

Among other conditions that may simulate bulla, bronchiectasis and congenital or acquired cysts should be borne in mind. Bronchiectasis, as a rule, may be recognized by the clinical picture. The typical locality and the multiplicity of the lesion in case of cysts is given by Brandner[5] as a diagnostic point.

Should emphysema be associated with pulmonary diseases such as tuberculosis, anthracosilicosis, abscess, atelectasis, etc., which produce increased density of the lung it will readily be appreciated that roentgenological diagnosis of bulla will be made more difficult if not impossible.

There is no known treatment for bulla of the lungs. Treatment should be directed toward the cure of the associated disease whenever such is possible.

SUMMARY

Bulla is a pathological entity caused by the confluence of two or more of the terminal elements of the bronchial tree. They may be found subsequent to any condition that interferes with normal respiratory mechanism that produces increased intra-alveolar pressure. A single bulla is a rarity: they vary in size from that of a large vesicle to that of a large grape fruit. There are two views as to the formation of bullae: both believe bullae to be the result

of the increased intra-alveolar pressure that is present. The distinction between bullae and blebs has been stressed. Bullae are by no means innocuous. There is no clinical sign or symptom characteristic of bullae. Diagnosis is nearly always made by means of x-rays and the differential points have been discussed. There is no known treatment of the condition.

RESUMEN

La vejiga del pulmón es un proceso patológico causado por la confluencia de dos o más de los elementos terminales del árbol bronquial. Vejigas pulmonares pueden aparecer como resultado de cualquier estado que impida el mecanismo respiratorio normal y que produzca hiperpresión intraalveolar. Es muy raro que haya una sola vejiga. Las vejigas varían del tamaño de una vesícula grande al de una toronja grande. Existen dos opiniones acerca de la formación de vejigas; pero ambas coinciden en que son causadas por la hiperpresión intraalveolar presente. Se recalca la distinción entre vejigas y ampollas. Las vejigas no son inofensivas. No existe signo o síntoma clínico que sea característico de vejigas. Generalmente se hace el diagnóstico mediante la roentgenografía y se ha discutido los puntos en el diagnóstico diferencial. No se conoce tratamiento alguno para este mal.

REFERENCES

1 Benjamin, B., and Childe, A. E.: "Localized Bullous Emphysema Associated with Pneumonia in Children," *Jour. Pedat.*, 15: 621-632, (Nov.) 1939.

2 Loeschke, H.: "Handbuch der Speziellen Pathologischen Anatomie und Histologie," *Hencke, F. & Leubarsch, O.*, v. 3, pt. 1, 1928.

3 Wiese, E. R., Heiken, C. A., and Charr, R.: "Multiple Giant Bullae Associated with Anthracosilicosis," *Amer. Jour. Roentgenol. & Radium Ther.*, 42: 186-192, (Aug.) 1939.

4 Von Hansemann: "Untersuchungen über das Enstehen des Lungenemphyses," *Zentralbl. f. Allgemein. Pathol. u. Pathol. Anat.*, 971, 1900

5 Brandner, R.: "Ueber das Bullose Emphysem," *Fortschr. a. d. Geb. der Roentgenstrahlen*, 61: 144-153, (Mar.) 1940.

6 Willcox, A., and Foster Carter, A. F.: "Spontaneous Pneumothorax Associated with Bullous Emphysema," *Lancet*, 2: 315-317, (Aug. 7), 1937.

7 Harris, H. J.: "Extensive Destruction of Lungs: Emphysema with Giant Bullae: Autopsy," *Radiology*, 36: 492-494, (April) 1941.

8 Edwin, G. S.: "Extreme Bulla Formation," *Brit. Jour. Tuberc.*, 31: 293-295, (Oct.) 1937.

9 Kjaergaard, H.: "Spontaneous Pneumothorax in the Apparently Healthy," (1922). Quoted by Freedman, Eugene,[11] *Amer. Jour. Roentgen.*, 35: 324-340, (Mar.) 1936.

10 "The Merck Manual of Therapeutics and Materia Medica," 7th ed., *Merck & Co.*, Rahway, N. J., 1940.

11 Freedman, Eugene: "Emphysematous Blebs and Bullae," *Amer. Jour. Roentgenol.*, 35: 324-340, (Mar.) 1936.

12 Laurell, H.: "Ein Beitrag zur Deuting der Sogenannten Ringshatten in den Lungen," *Acta. Radiol.*, 10: 72-119, 1929.

Nebulized Penicillin in the Treatment of Respiratory Infections

ROBERT J. HANKS, M.D., F.C.C.P.
Waco, Texas

The realm of drug therapy in treating bronchial infections has practically reached the limit of its usefulness and this has been apparent for many years. The same is true of parental injections, however, to a lesser degree; therefore the search has been for a more efficacious method of treatment.

The use of nebulized solutions seems to be the answer. This is not a new method, for it has been in vogue for quite sometime. Chevalier Jackson, twenty years ago advocated the instillation of drugs into the lungs *per se* through the bronchoscope, and this is still being done in lung abscesses where sulfa solution or penicillin is instilled into the abscess cavity itself, after aspiration of the pus. The results have been very good with this method. However, this treatment is rather severe from the patient's standpoint, and not everyone is adept enough to use the bronchoscope; so this method has limited usefulness.

The use of iodized oils applied to the bronchi by laryngeal instillation is in no sense a recent development. The inhalation of medicated vapors is an ancient and empirical method. The application of drugs having a special pharmacologic effect, as epinephrine, and the development of nebulizers which permit very fine sub-division of the solution, has opened the field for inhalation therapy and the results already produced have surpassed the previous treatment records by the more indirect methods.

Nebulized solutions in the treatment of bronchial conditions was first described by Stacey in 1943,[1] with a report of five cases treated. This work was corroborated by Applebaum in 1944,[2] with a report of fifty cases treated. Sodium sulfathiazole in 5 per cent aqueous solution was the drug used by each of these workers. Treatments were given once, twice, or three times a day in chronic bronchitis and bronchiectasis with good results. No ill effects were noted from the use of this drug. An interesting part of this treatment was the fact that although the sulfathiazole solution was nebulized into the lungs, there was apparently no absorption into the blood stream, for the blood at no time showed perceptible amount of the drug. However, complications can occur with the sulfas, in that sodium sulfathiazole or sodium sulfadiazine when

in contact with the mucous membrane separates into sulfathiazole or sulfadiazine and sodium hydroxide, the latter of which is toxic. This toxic reaction consists of discomfort and swelling of the nasopharyngeal mucous membrane. Also, these patients can be sensitized to sulfa drugs in the same manner that sulfa applied to the skin of certain individuals will sensitize them to further treatment with the drug. One case which received sulfa nebulization for a period of eight weeks, was rested for four weeks and when placed back on the treatment became severely dyspenic, cyanotic and went into coma with death ensuing in twenty-four hours. With the advent of this unhappy experience, sulfa has not been used again.

Considering the rich circulation of the lung tissue, there is probably no other way in which the desired concentration of drugs can be maintained within the mucous membrane of the bronchial tree, than by local application through the air passages themselves. There are few drugs that diffuse out of the blood in sufficient amounts to affect the composition of the bronchial secretions, but it is precisely in such locations that inhaled drugs exert their strongest reactions.

Since the fatality with nebulized sulfa, penicillin alone has been used in treatment. The results with this solution have been so much superior to sulfa that there is no need to use the latter with the danger of sensitization and possible death. Thus far no complications have been experienced with penicillin. Solutions in various strengths have been tried and a saline solution containing 500 Units per cc. seems to give the best results. It has been stated by the manufactures of penicillin that the solution deteriorates rapidly but this has been disproven,[3] for if kept in the refrigerator, the solution will remain potent for at least four months and maybe longer.

The method of nebulizing the solution is simple. An oxygen tank with a flow meter and humidifier is connected by a rubber tube to a DeVilbiss Nebulizer No. 40, 2 cc. of penicillin solution is placed in the glass nebulizer and an oxygen flow of four liters is set. The patient is instructed to hold the nebulizer between the teeth and breath through the mouth. The treatment usually takes twenty minutes, and is given once a day.

This new plan of treatment naturally gives the best results in the acute and sub-acute type of infection, but is also of a great deal of help to the chronic as well. Unfortunately, this last group of chronic bronchitis and bronchiectasis has been sadly neglected, mainly because of the lack of suitable therapy. No greater sin can be committed in therapy, than to pronounce a cough a case of bronchitis, assume a helpless and hopeless attitude and let it go at that. It is of no therapeutic value to give a bottle of cough

THERAPEUTIC RESPONSE	Number of Cases	No Improvement	Slight Improvement	Moderate Improvement	Marked Improvement
Acute Bronchitis	3	0	0	0	3
Bronchiectasis	6	1	1	2	2
Chronic Bronchitis	9	1	1	3	4
Sub-Acute Bronchitis	12	0	1	1	10
Acute Bronchitis	3	0	0	0	3
Acute-Tonsillitis and Laryngitis	4	0	0	0	4
	34	2	3	6	23

Slight Improvement: Satisfactory trend but not symptom free.

Moderate Improvement: Absence of findings except for occasional irritative cough and rales.

Marked Improvement: Total absence of all subjective and objective findings.

mixture to a patient with chronic bronchitis, for no cough mixture can cure this condition, nor will it give anything but very temporary relief. The above treatment will not cure these cases either, but, it will give them prolonged relief from a distressing cough, and their lives will be made more pleasant. They can be made comfortable and will remain thus until a respiratory infection strikes them and flares up the condition again. A few more treatments can be given, and again, they are comfortable.

In acute tonsillitis, laryngitis and bronchitis, the results are startling. One, two or three treatments give complete relief from fever, etc. The sub-acute type of infection, as the streptococcic pneumonitis, will respond to six to twelve treatments given once a day. The chronic infection will require twenty to sixty treatments taken once a day. In the chronic infections, the sputum will be reduced markedly, the temperature will return to normal, or nearly so and the toxic symptoms diminish and a feeling of well being will be re-established. Virus pneumonia will also respond to this method of treatment even where parental injection of penicillin has failed.

SUMMARY

1. A group of 34 patients with various respiratory infections was treated by the inhalation of a nebulized solution of penicillin, 500 units per cc.

2. Of the 34 cases, 32 or 94 per cent of the series received appreciable benefit.

3. The danger of sulfa sensitization is presented for further observation.

4. Penicillin in nebulized form offers a safe and efficacious method of treatment in respiratory infections, both acute and chronic.

608-609 Professional Bldg.

RESUMEN

1. Se trató a un grupo de 34 enfermos, con diversas infecciones respiratorias, por medio de la inhalación de nébulas de una solución de penicilina (500 unidades por cc.).

2. De los 34 casos, 32 o sea el 94 por ciento de la serie, obtuvieron apreciable beneficio.

3. Se presenta, para investigación adicional, el peligro de la sensibilización a los sulfonamidos.

4. La penicilina en forma de nébulas ofrece una terapéutica inofensiva y eficaz para las infecciones respiratorias, tanto agudas como crónicas.

REFERENCES

1 Stacey, John W.: "The Inhalation of Nebulized Solutions of Sulfonamides in the Treatment of Bronchiectasis," *Dis. of Chest,* 9: 302-306, (July-Aug.) 1943.

2 Applebaum, Irving L., Lt. Col.: "The Treatment of Bronchial Lesions by the Inhalation of Neublized Solutions of Sodium-sulfathiazole," *Dis. of Chest,* 10: 415-421, (Sept.-Oct.) 1944.

3 Levine, Max Major: "Penicillin Deterioration," Personal Communication.

A Tuberculosis Survey of a Rural Mountain County*

ELLIOTT P. SMART, M.D., F.C.C.P.**
ROBERT W. CLARKE, M.D.***
Murphys, California

This is to report the problems encountered in and the results of a survey which was conducted in a rural mountain county. Calaveras County lies on the west slope of the Sierra Nevada mountains between 1500 ft. and 4000 ft. elevation, and is almost 125 miles directly east of San Francisco. The principal means of livelihood are mining, timber, cattle raising, and cement manufacture. The county has lost some of its residents because of the war. The only increase in population has been in the lumbering communities. The population of towns D and F show the greatest influx. The towns of E and G are the principal mining communities (See Table 1).

The portable fluoroscope, supplied by the California Tuberculosis Association, was used. This was shipped to town "A" by rail from where it was transported by truck and set up in the other six communities, C, B, D, E, F, and G. It was necessary to assemble and dismantle the fluoroscope a total of seven times. This presented a problem in itself as the machine and equipment weighed a total of 1800 lbs. However, through the willingness and cooperation of the residents, this job and the job of transportation were efficiently accomplished without cost .

Data: The population of the county according to the 1940 census was 8221. A total of 993 persons were fluoroscoped. This is 12 per cent of the county population.

Table 1 shows the towns where the examinations were conducted. The percentage of persons fluoroscoped varies between 16 per cent and 24 per cent of the towns' populations. Of course, many fluoroscoped in the towns live in rural communities or on ranches. However, the percentage did not vary appreciably from town to town. Also the numbers of x-rays advised were about equally distributed in relation to the population of the respective towns. About 78 per cent of those who had suspected chest path-

---

*From the Bret Harte Sanatorium and Calaveras County Tuberculosis Association.
**Medical Director, Bret Harte Sanatorium, Murphys, California.
***Resident Physician, Bret Harte Sanatorium, Murphys, California.

ology from the fluoroscopic viewpoint and were advised by personal letter to have a chest x-ray film taken, accepted the advice and presented themselves at Bret Harte Sanatorium where all the films were taken and read.

Table 2 shows the breakdown of the population as estimated by persons conducting the survey. It will be seen that about one-half of the persons fluoroscoped were adults, and about two-thirds

TABLE 1

Towns	Population	Number fluoroscoped	Percent of town population fluoroscoped
A	450	72	16
B		96	
C	1150	208	18
D	400	95	24
E	1250	295	24
F	600	125	21
G	550	102	19
TOTAL	4400	993	
CALAVERAS CO.	8221		12

Towns	No. x-rays advised	No. x-rays taken	Percent x-rays taken of those advised
A	8	6	75
B	9	6	76
C	9	8	89
D	2	2	100
E	12	10	83
F	2	1	50
G	4	3	75
TOTAL	46	36	
CALAVERAS CO.			78

TABLE 2

School enrollment in Calaveras County:

Elementary	840
High Schools	287
TOTAL	1127

Estimated school children fluoroscoped:

Elementary	175
High Schools	240
TOTAL	410

Estimated adults fluoroscoped 578
(About 2/3 of these never fluoroscoped before.)

of them had never been fluoroscoped before. This was encouraging because it brought in a new group.

Table 3 lists the findings of the thirty-six films taken. One minimal case was discovered in a seventeen year old High School student. This was considered tuberculosis because a film taken one month later showed no change and the Mantoux test was highly positive to First Strength P.P.D. Tuberculin. A film taken three months later showed an increase in the lesion. Of the four listed as "questionable tuberculosis," one was referred to his local physician. The remaining three and the two "questionable silico-tuberculosis," all had negative sputa culture examinations, except one who has failed to send in sputum specimen as requested.

Table 4 shows results of laboratory work. No sputa or gastric washings were found positive for tubercle bacilli.*

Table 5 shows the number of miles it was necessary to transport the scope between the towns, and the number of miles the persons conducting the survey had to travel. It shows the number of hours spent in actual fluoroscoping. It will be noticed that because of the size of the county and terrain, about one-half of the total hours spent were in travel.

*The one active case continued to progress, and positive sputum was finally obtained. Pneumothorax has been instituted.

TABLE 3

Fluoroscopic examinations		993
X-ray advised		46
X-rays taken at Bret Harte		36
Negative for pathology	9	
Advised recheck in one year	6	
Calcifications	8	
Questionable tuberculosis	4	
Minimal active tuberculosis	1	
Questionable silico-tuberculosis	2	
Pleurisy with effusion, healed	1	
Questionable heart disease	3	
Scoliosis	2	
TOTAL	36	

TABLE 4

Laboratory

Persons advised to have sputum examined	6
Persons whose sputum or gastric contents examined	5
Sputum examinations, smear and concentrated	4
Gastric contents cultured	7
Positive sputum, concentrated and cultured	0
Positive gastric contents	0

Table 6 shows the cost of the survey. This made the individual cost 50½ cents per person fluoroscoped. Such a cost may seem excessively high, but with the number of miles it was necessary for the personnel to travel, and the time this consumed owing to the type of community, it may be readily understood. If the travel time were eliminated, the salary would be reduced to about half, and then the cost per person would be between 25 and 30 cents.

Comment: Such a survey has been conducted each year in Calaveras County, beginning in 1941. Each year the number fluoroscoped has increased. This is the first year that an active case of pulmonary tuberculosis has been found. It may seem then, that such a survey is unnecessary. However, we feel it is of value, if for no other reason than that it makes the citizens tuberculosis-conscious. This was especially noted in the school children, who have been fluoroscoped for three years. The annual fluoroscoping has now become a routine which the children expect. This same trend was noted in the adults who had been fluoroscoped previously.

Since those conducting the examination sometimes worked at a leisurely rate, they could often talk individually to the people, and in this way learn much about the attitude on such a project.

Several problems frequently presented themselves. One of these was the fact that parents willingly brought their children to be examined, but would refuse to be fluoroscoped themselves. The remark often expressed was, "if I have something wrong with my chest, I don't want to know about it." Such an attitude can be overcome by pointing out the potential danger to their children and others if an unknown lesion should be present .Another prob-

TABLE 5

Number of miles scope transported within county	121
Total miles traveled (one auto)	844
Total person-miles traveled	1688
Number work hours:	
Doctors	61
Nurses	61
Number travel hours:	
Doctors	63
Nurses	63

TABLE 6

Rental of fluoroscope	$ 43.86
Salaries and travel expenses	440.00
Sputum studies	0.00
X-rays and postage	18.00
	$501.86
Cost per person	$ .50½

lem which should be solved is educating the public to the fact that the survey is being conducted free, that it is a reputable endeavor, and the examination requires only a few minutes of their time. In this same connection, the fact that the women do not have to disrobe should be made known. These facts should be emphasized through the various channels of publication used in propagandizing the survey.

It should be pointed out too, that one examination in which no tuberculosis is found does not insure a clean bill of health for life, but rather, frequent examinations are desirable.

Lastly, and we feel this is very important, there is the necessity of educating the citizens to the idea that an examination with no positive findings is just as valuable to that individual as one with pathology, and will give him satisfaction in the knowledge that he does not have active tuberculosis.

CONCLUSIONS

1. Citizen cooperation is essential for success of tuberculosis survey in a rural type of community.
2. A relatively large percentage of the population of such a county can be reached.
3. The follow-up with x-ray and sputa examinations can be very good.
4. Active tuberculosis is not prevalent in our county.
5. Travel time consumed one-half of the total time spent, and this fact increased the cost per examination.
6. The cost per person fluoroscoped was 50½ cents.
7. It is possible to make the examination more personal in such a community.
8. Better education of the public is necessary.

CONCLUSIONES

1. Es esencial la cooperación del público para el buen éxito de censos de tuberculosis en una colectividad de tipo rural.
2. En tal colectividad puede alcanzarse a un porcentaje de la población relativamente elevado.
3. La observación subsecuente con radiografías y exámenes de esputo puede ser muy satisfactoria.
4. No prevalece la tuberculosis activa en nuestra colectividad.
5. La mitad del tiempo se empleó viajando, y ésto acrecentó el costo por examen.
6. El costo fue 50.5 centavos por cada persona radioscopiada.
7. En tal colectividad es posible hacer el examen de manera más individual.
8. Es necesaria una mejor educación del público.

Bronchial Asthma

(A Case Report)

ISRAEL KAUFMAN, M.D., F.C.C.P.
Brooklyn, New York

The following is a case report of a patient with severe bronchial asthma of infectious origin who was relieved of her symptoms by the administration of Penicillin Sodium.

Miss M. B., a white female, aged 34 years, came to my office on April 27, 1942, complaining of severe asthmatic attacks for the "past thirteen years." These attacks lasted throughout the year and were characterized by wheezing, cough, shortness of breath, and orthopnea. She stated that she was never free of the attacks, but did have periods when the attacks were less severe. She had to take from one to six injections of Adrenalin Hydrochloride (one cc. each) a day. When the conditions permitted, she would try to do without the Adrenalin. This, however, was rare. She gave a history of a sore throat thirteen years ago (1929) and following that episode she went to a doctor who attempted to remove her tonsils by electro-coagulation. After the first treatment she developed severe asthma. She never returned for further treatments. She also noticed that each time that she "caught a cold her asthmatic attacks would be more severe." At such times she would be bedridden and in need of almost constant medical care.

The physical examination revealed a well developed and well nourished young white female, moderately dyspnoeic, and coughing throughout her visit in my office. The cough was deep seated and harsh. It was generally unproductive although the patient stated that at times she brought up copious amounts of white frothy sputum. She was 5 ft. 3 inches in height and weighed 193 lbs. She stated that she had always been stout. On examination, the only positive findings were,—a pale nasal mucosa, a pair of enlarged cryptic tonsils, wheezing throughout the entire chest. Blood pressure of 130 systolic and 90 diastolic, pulse 92/min. and respiration 38/min. The patient was alert, well oriented and apparently not toxic. Her skin was clear and she never had any eruptions.

A tonsillectomy was advised and she consented. She was admitted to the hospital and the tonsillectomy was performed under local anesthesia (1% Novocaine with 1:1000 Adrenalin Hydrochloride). This was done on June 30, 1942 and the patient was free of attacks until July 30, 1942. At that time she cought a cold and had an attack immediately. We then decided to administer cold vaccine to immunize her against her apparent sensitivity. A stock vaccine was obtained and administered in graded doses, starting with 0.05 cc. An area of redness was seen at the site of the injection within one hour, but there was no pain or discomfort. The doses were given on alternate days, intramuscularly, in increasing amounts (adding 0.05 cc. to the previous dose) until 0.5 cc. was reached. During this time, her discomfort was mild and the patient did not resort to Adrenalin injections. However, all exertion still produced marked dyspnoea. Treatment was discontinued in January 1943 because of maximum benefit. The patient felt better than when she first came to

me but she was not well. In October 1943, she had another severe attack during which she did not respond to Adrenalin and it became necessary to administer 7.5 grains of Aminophylin intravenously. The relief was immediate, but the patient had a severe coughing spell following the injection. At this time she was given a prescription calling for Ephedrine Sulphate gr. 3/8, Phenobarbital gr. 1/2 and Syrup of Wild Cherry q.s. to Drachms one. This was to be taken every four hours. The results so far were not too satisfactory and in October 1944 we again decided to try to desensitize the patient. This time Pertussis Vaccine was used in conjunction with Histamine. The injections were given separately, one in each deltoid region, at five day intervals, and in doses graded from 0.1 cc. for the pertussis vaccine increasing each dose by 0.1, while the Histamine was administered in smaller doses ranging from 0.01 to 0.015 to 0.02, etc. After the fifth injection the patient reported that she did not have any attacks for an entire five day period. During this five day period she did not wheeze. By this time we had reached the maximum dose for the vaccine (0.5 cc.). The injections were continued and the patient had remissions of varying lengths of time, ranging from six to nine days during which she was perfectly comfortable. However, she caught cold again in January 1945 and we decided to try an autogenous vaccine made from the nasal and throat secretions. The results from the autogenous vaccine were most unsatisfactory and were discontinued abruptly when the patient suffered a sudden and serious attack at the end of January 1945. At this time she again required Aminophylline intravenously. This was the worst attack thus far. Two days later she had another, even more serious attack which did not respond to Aminophylline and the patient was hospitalized.

The patient was brought to the hospital on February 3, 1945. She was extremely dyspnoeic and orthopneic. Her temperature was elevated to 100.8° F, pulse 100 and respiration 40 per minute. Her blood count showed 5,200,000 red cells, 13,400 white cells with a differential count of 65 per cent P.M.N., 32 per cent lymphocytes, 3 per cent Eosinophiles. On admission she was given an ampule of Aminophylline (7.5 gr.) intravenously to relieve the spasm. The following morning Penicillin Sodium was administered in 10,000 unit doses intramuscularly, every two hours. The patient felt better on the third day of her stay in the hospital or after 240,000 units of the Penicillin had been administered. She was discharged from the hospital after 500,000 units had been given and permitted to administer the medication at home under my supervision. Her use of the hypodermic needle and syringe in the administration of the adrenalin permitted of this procedure. We continued the medication until 1,900,000 units had been administered. The last dose of Penicillin was administered in the last week of February and the patient has not had any attacks since then (March 1, 1945 to May 9, 1945). The patient has returned to work and is very comfortable. There is no wheezing and very little discomfort on exertion. Since then her basal metabolic rate has been estimated and found to be minus 38. The patient was put on a reducing diet with small doses of thyroid extract. Her weight has been reduced from 178.0 lbs. in February to 163 lbs. in May.

RESUME

The patient was apparently sensitised to some bacterial protein when the electrocoagulation was attempted. The presence of the

infected tonsils was a constant source of allergens. The presence of the tonsils fifteen years after the first attack permitted the spread of the infection to the regional lymph glands so that the removal of the tonsils did not remove the cause of the asthmatic attacks. We feel, therefore, that the administration of the Penicillin did clear up the residual infection and the patient is now free of her bronchial asthma.

3608 Bedford Avenue.

RESUMEN

Aparentemente se sensibilizó al paciente a alguna bacterioproteína cuando se intentó la electrocoagulación. La presencia de las amígdalas infectadas fue una fuente constante de alergenos. La presencia de las amígdalas por quince años después del primer ataque motivó la propagación de la infección a los ganglios linfáticos regionales, de modo que la extirpación de las amígdalas no eliminó la causa de los ataques asmáticos. Creemos, por consiguiente, que fue la administración de penicilina la que acabó con la infección residual y ahora la enferma está libre de su asma bronquial.

The Tuberculosis Problem of the Union of South Africa

DAVID P. MARAIS, M.D., F.R.C.P. (Edin.), F.C.C.P.
Cape Town, South Africa

The pattern of tuberculosis in the Union of South Africa is modified by a number of factors, some ethnologic, some climatic, some industrial, and some, to a lesser extent, geographic. Introduced into virgin soil by sufferers from Europe seeking the sun-drenched highlands of the Karroo plateaux, the infection spread amongst the mixed coloured and native sections, the servant class of worker, and from them to the families in which they served. Records and statements, however, show that 60 or 70 years ago the Native territories were already tuberculised. The rapid development of gold mining attracted a large labour corps of natives (Bantu) who soon became infected under the conditions of deep-level mining in silica-rich quartz and an infection by European skilled miners who had emigrated from the rain and fog of Europe. The return to their homes in the native reserves still further spread the infection; meanwhile the de-tribalised native sickened and died in the poor quarters and suburbs of the big cities leaving a focus of heavy infection wherever he stayed.

The South African born white, a composite European national—basically Dutch, French, English, etc., like the United States citizen—had lost some of his resistance by the rarity or complete absence of tuberculous contacts in the early half of his three century occupation of the land, and now finds himself and his children struggling against a rising tide of infection in the large modern centres, and even in his farm homes from tuberculous domestic servants. His tissue reaction against tuberculosis differs slightly from that of his recently arrived cousin from Europe, and his adjustment to the modern conditions of overcrowding and speed is slowly and painfully taking place.

These facts one can find partly reflected in the mortality returns which, although reasonably accurate for the white (European), are mere estimates as regards the non-European (coloured, native and Asiatic), since outside a dozen or so large urban centres no statistical returns have been available for many years, a reflex consequence of false Union economy.

Certain findings emerging from tuberculosis surveys and special reports are worth mentioning for comparison with a similarly mixed population in the United States. Thus we note a consist-

ently high ratio in the tuberculosis mortality varying from 10:1 to 5:1 amongst mixed coloured and whites in the same community.

Ignorance of food values and especially of protective food factors, bad housing, thriftlessness and alcoholism overburden the scale already loaded down by his poorer fighting powers to produce this ratio in his disfavor.

In the case of the pure native (Bantu) returning home to his kraal, with his tuberculous legacy from his work in the big cities or the deep gold mines, it is interesting to note that within two generations, 50 years, since the opening of the mines, the average type of tuberculosis has changed from the early "childhood type" or the acute pneumonic to the fibro-caseous, cavernous and even the fibroid type, indicating a definite rise in the grade of resistance.

One South African worker, Dr. Dormer, Medical Superintendent of the King George V Tuberculosis Hospital in Durban, insists that race is not a factor in determining the fatality of tuberculosis. His observations lead him to conclude that diet is an important conditioning factor and if to this we add sustained physical effort, and a bad (overcrowded) environment, the balance is loaded against the recovery from an initial infection. Just as Sander (Saranac Lake Symposium, 1941) discussing the Charleston records believes that the Negro slaves suffered an increase of tuberculosis when their stable and well-organized existence gave place to a loss of economic security following their freedom, so does Dormer believe that the exchange of the primitive, care-free and easy life of the South African native in his reserves for the crowded, high-pressure and undernourished conditions of the modern labour centres has meant a strain under which his early tuberculous infection develops more frequently into progressive disease than if his primitive conditions had remained unchanged.

He quotes in support certain findings:

1. A high percentage of infection in Native kraals in the rural areas, and very little disease.
2. The same type of disease in European infants and native infants.
3. The type of disease nowadays found in rural Native areas is very like the European.
4. The tendency towards the occurrence of the so-called primitive type of disease in Europeans in the city of Vienna after the strain and exhaustion of the last Great War.

The control of tuberculosis is then in large part related to the control of the non-European (coloured, Bantu and Asiatic) tuberculotic. Measures in operation at present are sporadic and far from a properly organized campaign, since no large scale policy has yet been accepted.

True it is that in the Miners' Phthisis Bureau (for the detection of Silicosis and Silico-Tuberculosis) in Johannesburg, we have the finest institute of its kind and one which has produced astonishing results, and a working pattern for all similar institutes elsewhere; but in the realm of pure tuberculosis we are not agreed nor ready to shoulder the cost of an effective and comprehensive campaign. Moreover, the Union Parliament is at present debating the outlines of a National Health Service which would provide a free medical service on carefully organized and generally socialized lines.

Nevertheless, we have a skeleton scheme to work upon. Thus we have notification of the disease, though still very imperfect; we have three large and flourishing Preventoria for child contacts financed entirely by the Christmas Stamp Fund, and six Tuberculosis Hospitals and Sanatoria scattered throughout the four Provinces of the Union. In only one centre, Cape Town, have we achieved some co-ordination between city tuberculosis clinics, a voluntary Tuberculosis Care Committee and the various elements of a Municipal scheme under the control of the Medical Officer of Health, including clinics or examination centres, hospital, sanatorium, rehabilitation centre and Preventorium.

The geographical distribution of Tuberculosis with high incidence in the coastal cities and towns, and steadily increasing incidence in the densely populated mining areas, complicates the control while the malnutrition, due largely to lack of protective food substances prevalent in labour groupings scattered throughout the country even in the "ideal" climate of the dry high-level plateaux, has recently been found to be an important factor.

Large scale group tests by Tuberculin have only explored certain small sections of the field, e.g., student nurses in Cape Town, mental hospitals (Union) (71 per cent positive of 5,164 tested), Dr. P. Allan's survey in the native territories (66 per cent of 6,508 tested) and some tests by Dr. B. A. Dormer in Natal, natives showing 50 per cent to 85 per cent positives according to age.

Mass radiography by miniature film is available as yet only in Johannesburg (the gold mining centre) and in Durban, but the intervention of war has held up the projected schemes for Cape Town and other centres.

In summary the following figures may help the American reader to visualize the size of our South African problem.

Population of the Union of South Africa in round figures. Estimates based on the Census of 1936

European (whites)	2,250,000
Coloured (mixed)	800,000
Asiatic (Indian mostly)	220,000
Bantu (original Natives)	7,000,000

Territory of the Union of South Africa: 473,000 square miles, the equivalent of the area of Texas, California and Louisiana combined.

Annual Deaths:	European	750
	Non-European	15,000 (estimated)

Tuberculosis cases (infectious) discoverable by all methods of examination, including mass radiography, *requiring treatment*, Dormer's estimate, based on 1936 Census Returns:

European	(2 positive spitters per 1,000)	4,000
Coloured	(4 positive spitters per 1,000)	3,140
Asiatic	(4 positive spitters per 1,000)	860
Bantu	(4 positive spitters per 1,000)	24,000

Existing Beds for Treatment

For European	515
For Coloured (Asiatic and Bantu)	2,000

Present Expenditure on Tuberculosis (1942-43)

NOTE: * Pound Sterling.

*198,028 or about $792,000 with a Capital Investment on buildings and equipment of *250,000 or about $1,000,000.

Beds still required for an adequate Tuberculosis Control Scheme

	Capital Cost	Annual Maintenance
European	550 at 800 a bed — *444,000	*730,000
Coloured	3,140 at 400 a bed — *800,000	*570,000
Asiatic	880 at 250 a bed — *200,000	*160,000
§Bantu	2,000 at 100 a bed — *200,000	§*880,000

§It is to be noted that of 24,000 estimated cases only 20 per cent are treatable in hospital. Eighty per cent would refuse hospital control but would be amenable to control at centres in the Native reserves where inexpensive methods could operate successfully as has already been proved in severe malaria epidemics.

Note: For rough calculation *1 may be considered the equivalent of $4.

Total Cost of Beds still required: *1,644,000 or about $6,576.000.

Annual Expenditure in running the Scheme: *2,340,000 or about $9,360,000, being an 8-fold increase on existing expenditure in Capital Costs and a 9-fold increase in Annual Expenditure.

The magnitude of the costs may compel gradual operation under which *1,000,000 capital outlay and *1,000,000 annual expenditure may be easily supported.

The latest and most comprehensive account for the whole question is to be found in a paper in the "Proceedings of the Transvaal Mine Medical Officers' Association," by Drs. Dormer, Friedlander and Wiles, Nov., 1943:

1. Eliminate the infecting case—find, isolate, treat.
2. (a) Feed an adequate diet to all sections of the community.
   (b) Do not allow sustained physical effort without adequate diet.

Case finding would depend on mass radiography operating in clinics established as well as mobile. Isolation and treatment would

occur on well-known and accepted lines. The pasteurizing of urban milk supplies would be compulsory in order to eliminate an existing heavy bovine infection. Emphasis is finally laid on the education of the whole people, especially in diet selection with regard to protective foods, and also on the importance of conditioning the potential labourer by good feeding and physical training before submitting him to the severe tax which modern labour places on his strength and resistance.

The problem at present hinges largely on finance, that is, on how much the small body of taxpayers amongst two and a quarter million white people can bring themselves to afford. One feels that a really big effort now may achieve remarkable results. Let us pray that the "powers that be" may be stirred to action in time.

SUMMARY

The pattern of tuberculosis in the Union of South Africa is modified by a number of factors: ethnologic, climatic, industrial, and, to a lesser extent, geographic.

The control of tuberculosis is in large part related to the control of the non-European (coloured, Bantu and Asiatic) tuberculotic. Measures in operation at present are sporadic and far from a properly organized campaign.

The objectives to be achieved can be summarized as follows:

1. Eliminate the infecting case—find, isolate, treat.
2. (a) Feed an adequate diet to all sections of the community.
   (b) Do not allow sustained physical effort without adequate diet.

Case finding would depend on mass radiography operating in clinics established as well as mobile. Isolation and treatment would occur on well-known and accepted lines. The pasteurizing of urban milk supplies would be compulsory in order to eliminate an existing heavy bovine infection. Emphasis is finally laid on the education of the whole people, especially in diet selection with regard to protective foods, and also on the importance of conditioning the potential labourer by good feeding and physical training before submitting him to the severe tax which modern labour places on his strength and resistance.

The problem at present hinges largely on finance, that is, on how much the small body of taxpayers amongst two and a quarter million white people can bring themselves to afford. One feels that a really big effort now may achieve remarkable results. Let us pray that the "powers that be" may be stirred to action in time.

101 St. George's Street.

RESUMEN

El patrón de la tuberculosis en la Unión del Africa del Sur está modificado por un número de factores: etnológicos, climáticos, industriales y, en menor grado, geográficos.

El control de la tuberculosis está relacionado, en gran parte, con el control del tuberculoso no europeo (de color, Bantú y asiático). Las medidas operativas en la actualidad son esporádicas y están lejos de constituir un plan debidamente organizado.

Los objetivos por alcanzar pueden resumirse en la forma siguiente:

1. Eliminar el caso infeccioso—Descubrirlo, aislarlo, tratarlo.
2. (a) Proporcionar una dieta adecuada a todas las secciones de la colectividad.
   (b) No permitir trabajo físico prolongado sin una dieta adecuada.

El descubrimiento de casos dependería de exámenes radiográficos colectivos funcionando en clínicas tanto fijas como móviles. El aislamiento y tratamiento se llevarían a cabo de acuerdo con métodos bien conocidos y aceptados. La pasterización de la leche en los centros urbanos sería obligatoria a fin de eliminar la considerable infección bovina existente. Finalmente se hace hincapié sobre la educación de todo el pueblo, especialmente en la selección de la dieta con respecto a los alimentos protectores, y también en la importancia de preparar al trabajador potencial mediante la alimentación y el entrenamiento físico antes de someterlo al riguroso esfuerzo que el trabajo moderno requiere de sus fuerzas y resistencia.

En el presente el problema depende mayormente del asunto monetario, es decir, de la cantidad de dinero que la pequeña parte de contribuyentes entre los dos millones y un cuarto de gente blanca pueda persuadirse a suministrar. Creemos que un esfuerzo verdaderamente grande podría ahora alcanzar resultados extraordinarios. Roguemos que pueda incitarse a las autoridades a actuar a tiempo.

Editorial

SPECIALTY BOARDS

The members of the American College of Chest Physicians have spoken. Through their established Chapters they have proposed by resolution and petition to the Board of Regents of the College that appropriate steps be taken to organize an American Board of Diseases of the Chest. The issue is of paramount importance and the mandate is clear.

The Board of Regents of the College has been of the opinion that any action taken to organize an American Board of Diseases of the Chest should be in the nature of a joint movement of all of the societies concerned with this specialty.

With this objective in mind, the American College of Chest Physicians in 1943 appointed a committee to make a study of the problems involved and report its findings to the Board of Regents of the College.

In November 1944, committees representing the American Association for Thoracic Surgery, the American Bronchoesophagological Association and the American College of Chest Physicians met at St. Louis to discuss this matter. Following a thorough discussion of the many problems involved, a resolution was adopted recommending that the interested societies discuss the matter with the members of the Advisory Board for Medical Specialties.

At Buffalo, New York, on June 10, a committee of the College will meet with the Executive Council of the American Trudeau Society to discuss joint action to establish an American Board of Diseases of the Chest. The chest specialists are deeply interested in the success of this meeting.

There are approximately 2,000 physicians eligible for certification in the specialty of chest diseases. At the present time there are 15 Boards which are recognized by the Council on Medical Education of the American Medical Association and the Advisory Board for Medical Specialties. Less than half of these Boards have more than 2,000 certificants; some of the Boards have fewer than 200.

Would it not tend to defeat the plan of certification if a large group of physicians who are engaged in a medical specialty are denied the same recognition accorded to other groups? Certainly, no important specialty would willingly submit to be relegated to a position of subordination; commonly referred to as a "sub-specialty". Certainly, no reputable physician wishes to be classified or known as a sub-specialist.

If the Specialty Boards are to serve the purpose for which they have been organized, it is essential that they be reviewed from time to time and that they be adjusted to meet changing conditions.

It is our hope that the leaders in our medical societies will keep in step with scientific progress; for to retrogress is to invite disaster.

J. A. M.

Twelfth Annual Meeting

AMERICAN COLLEGE OF CHEST PHYSICIANS

Hotel Sir Francis Drake, San Francisco

JUNE 27 - 30, 1946

P R O G R A M

THURSDAY, JUNE 27

8:00 A. M. Registration

9:00 A. M. Administrative Sessions

Meeting, Executive Council
Meeting, Board of Governors
Meeting, Councils and Committees

9:00 A. M. Scientific Session

Refresher Course on Diseases of the Chest
Sponsored by the California Chapter,
American College of Chest Physicians
R. H. Sundberg, M.D., San Diego, *Chairman*

Pneumonias and Their Complications
Edwin L. Bruck, M.D., Professor of Medicine,
University of California, San Francisco

Bronchiectasis
J. J. Singer, M.D., Director, Research,
Rose Graff Foundation, Los Angeles

Lung Abscess (Surgical Aspects)
Paul C. Samson, M.D., Assistant Clinical Professor of Surgery,
Stanford University, San Francisco

Tumors of the Lung
John C. Jones, M.D., Los Angeles

General Discussion

12:00 Noon Luncheon Meeting

California Chapter, American College of Chest Physicians
Stephen A. Parowski, M.D., San Diego, President, *presiding*

(Guest speaker to be announced)

Business Meeting

Election of Officers

2:00 P. M. *Meeting, Board of Regents*

2:00 P. M. *Scientific Session*

Refresher Course on Diseases of the Chest
Sponsored by California Chapter,
American College of Chest Physicians
John C. Sharp, M.D., Salinas, *Chairman*

Relationship of Tuberculosis to Cardiac Disease, Stressing the Importance of Cor Pulmonali
Marion J. Read, M.D., Clinical Professor of Medicine,
University of California, San Francisco

Minimal Tuberculosis and Its Therapy
C. Gerald Scarborough, M.D., Medical Director,
Santa Clara County Hospital, San Jose

Surgical Therapy of Tuberculosis
William L. Rogers, M.D., San Francisco

Chemotherapy in Tuberculosis
Benjamin L. Freedlander, M.D., Harold Brunn Research Institute,
Mt. Zion Hospital, San Francisco

General Discussion

6:30 P. M. *Dinner, International Night*

Chevalier L. Jackson, M.D., Philadelphia, Pa., *Chairman*,
Council on Pan American Affairs, *presiding*

Co-Chairmen:

Andrew L. Banyai, M.D., Milwaukee, Wis., *Chairman*,
Council on European Affairs

Harry C. Warren, M.D., San Francisco, Cal., *Chairman*,
Council on Pan Pacific Affairs

Penicillin in Acute Supurations of the Lung
Donato G. Alarcon, M.D., Regent for Mexico, Mexico City

College Activities in Canada
William E. Ogden, M.D., Regent for Canada, Toronto

Report of the Greek Chapter of the College
Peter A. Theodos, M.D., Athens, Greece, Member,
Council on European Affairs

College Progress in South Africa
David P. Marais, M.D., Governor of the College for
South Africa, Cape Town

China's Plans for Re-building Her Medical Facilities
Shu Fan Li, M.D., Governor of the College for China, Hong Kong,
Member of the Council on Pan Pacific Affairs

Bilateral Collapse in Pulmonary Tuberculosis
Miguel Jimenez, M.D., Mexico City

Oxidase and Tuberculosis
Paulo Seabra, M.D., Dio de Janeiro, Brazil

The Eradication of Tuberculosis; The Greatest Health Problem in the Philippines
Manuel Quisumbing, M.D., San Pablo, Philippine Islands

FRIDAY, JUNE 28

9:00 A. M. Administrative Session

Report of the Secretary-Treasurer
Report of the Executive Secretary
Reports of Councils and Committees
Election of Officers
New Business

12:00 Noon Luncheon Meeting

Annual Conference of College Chapter Officials
Alvis E. Greer, M.D., Houston, Texas, *Chairman, presiding*
Arthur Q. Penta, M.D., Schenectady, N. Y., Secretary

Forum on College Activities

Participants:

E. W. Hayes, M.D., Monrovia, Cal., *Chairman,*
Council on Undergraduate Medical Education

J. Winthrop Peabody, M.D., Washington, D. C., *Chairman,*
Council on Postgraduate Medical Education

C. M. Hendricks, M.D., El Paso, Texas, *Chairman*
Council on Military Affairs and Public Health

James H. Stygall, M.D., Indianapolis, Indiana, *Chairman,*
National Council of Tuberculosis Committees

Benjamin L. Brock, M.D., Oteen, N. C., *Chairman,*
Council on Sanatorium Standards and Administration

Robert E. Duncan, Captain, U.S.N., Bethesda, Md., *Chairman,*
Membership Committee

Andrew L. Banyai, M.D., Milwaukee, Wis., *Chairman,*
Committee on State Laws for Tuberculosis

Louis Mark, M.D., Columbus, Ohio, *Chairman,*
Committee on Occupational Diseases of the Chest

Edwin R. Levine, M.D., Chicago, Illinois, *Chairman,*
Committee on Management & Treatment of Diseases of the Chest

Jay Arthur Myers, M.D., Minneapolis, Minn., *Editor-in-Chief,* College Journal, "Diseases of the Chest"

J. C. Placak, M.D., Cleveland, Ohio, *Chairman,* Board of Regents

William A. Hudson, M.D., Detroit, Mich., *Chairman* Board of Governors

NOTE: Each speaker will be limited to five minutes

General Discussion

Election of Officers

2:00 P. M. *Scientific Session*

Inhalation Therapy in Bronchial Infections
Edwin R. Levine, M.D., Chicago, Illinois

Hazards of Bovine Tuberculosis as a Matter of Public Health Significance, and a Potential Human Lung Infection with the Bovine Tubercle Bacilli
H. M. O'Rear, M.D., Sacramento, California

Clinical Applications of Topographic Anatomy of the Bronchi and Lungs
Chevalier L. Jackson, M.D., John F. Huber, M.D., and Charles M. Norris, M.D., Philadelphia, Pennsylvania

Inhalation of Carbon Dioxide for the Management of Cough
Andrew L. Banyai, M.D., Milwaukee, Wisconsin

Observations on Cystic Emphysema of the Lungs
Major E. Korol, M.C., Batavia, New York

5:00 P. M. *Meeting, Board of Regents*

8:00 P. M. *X-Ray Conference*

G. N. Pierce, M.D., San Francisco, California, *presiding*

Physicians who wish to present x-ray films should send their films plus a resume of the history, physical findings, significant laboratory work and autopsy or surgical findings, to Dr. G. N. Pierce, 450 Sutter Street, San Francisco 8, California.

The Committee will have slides made of those films which are selected for the Conference. The slides will be projected on a large screen so that they will be easily visible to the entire audience. Your kind cooperation in forwarding the films and other data to the Chairman of the Conference, will be very much appreciated.

SATURDAY, JUNE 29

9:00 A. M. *Examinations for Fellowship (Oral)*

9:00 A. M. *Scientific Session*

Treatment of Tension Cavities with Pneumothorax
I. D. Bobrowitz, M.D., Otisville, New York

Treatment of Complications Arising During the Course of Collapse Therapy for Pulmonary Tuberculosis
Comdr. Morton R. Gibbons, U.S.N., Corona, California

A Critical Study of Pneumoperitoneum and Phrenic Nerve Crush in Pulmonary Tuberculosis
Allan Hurst, M.D., H. M. Maier, M.D., and
Ralph Dwork, M.D., Denver, Colorado

The Significance of the Time Element in Tuberculous Infiltrations
Herbert A. Burns, M.D., St. Paul, Minnesota

B. C. G. Vaccination Among Indians
J. D. Aronson, M.D., Washington, D. C.

12:00 Noon *Luncheon Meeting*

Conference of Medical Directors and Superintendents
Benjamin L. Brock, M.D., Oteen, N. C., *Chairman,*
Council on Sanatorium Standards and Administration, *presiding*

Tuberculosis Sanatorium Standards
J. Winthrop Peabody, M.D., Washington, D. C.

General discussion of problems which concern medical directors and superintendents of tuberculosis hospitals and sanatoria

Election of Officers

2:00 P. M. *Examination for Fellowship (Written)*

2:00 P. M. *Scientific Session*

Reconditioning Following Thoracic Surgery in the Tuberculous Patient
O. Leonard Huddleston, M.D., Los Angeles, California

Immobilization of Both Lungs by the Equalizing Pressure Chamber in Pulmonary Tuberculosis
Alvan L. Barach, M.D., New York, New York

Evidence of the Efficacy of Streptomycin in Experimental Tuberculosis
W. H. Feldman, M.D., and H. C. Hinshaw, M.D., Rochester, Minn.

Clinical Use of Streptomycin in the Treatment of Tuberculosis
K. H. Pfuetze, M.D., Cannon Falls, Minnesota, and
H. C. Hinshaw, M.D., Rochester, Minnesota

6:30 P. M. Dinner

"Information Please in Medicine"

Carl H. Gellenthien, M.D., Valmora, New Mexico, *Moderator*

Panel of Experts:

Medicine:

James J. Waring, M.D., Professor of Medicine,
University of Colorado, Denver, Colorado

Surgery:

Alton Ochsner, M.D., Professor of Surgery,
Tulane University, New Orleans, Louisiana

Pathology:

Emil Bogen, M.D., Pathologist,
Olive View Sanatorium, Olive View, California

Roentgenology:

(To be announced)

Bronchoscopy:

Paul C. Samson, M.D., Assistant Clinical Professor of Surgery,
Stanford University, San Francisco, California

Physicians who wish to submit questions to the experts should mail them promptly to the Executive Officers of the American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois. Questions which are accepted will be published in "Diseases of the Chest" together with the answers.

SUNDAY, JUNE 30

9:00 A. M. Scientific Session

Patent Ductus Arteriosis; Present Surgical Status
J. W. Nixon, M.D., San Antonio, Texas

Thymectomy in the Treatment of Myasthenia Gravis
Ralph Adams, M.D., and Frank Allan, M.D., Boston, Massachusetts

Mediastinal Tumors
Brian B. Blades, M.D., Washington, D. C.

Surgical Treatment of Tuberculoma of the Lung
Colonel John B. Grow, M.C., Denver, Colorado

12:00 Noon Luncheon Meeting

Conference of Tuberculosis Committees
James H. Stygall, M.D., Indianapolis, Indiana, *Chairman*,
National Council of Tuberculosis Committees, *presiding*

State and Local Problems in Tuberculosis Control
Herman E. Hilleboe, M.D., Washington, D. C.

General Discussion

Election of Officers

2:00 P. M. Scientific Session

Experiences in the Pacific Theatre with Air Evacuation of Patients Suffering from Wounds of the Chest
Captain Leon B. Carson, U.S.N., Norfolk, Virginia

The Surgical Treatment of Bronchial Adenoma
Alfred Goldman, M.D., San Francisco, California

The Tuberculous Veteran, Plans for his Future Care
Colonel Roy A. Wolford, M.C., Washington, D. C.

An Objective Evaluation of the Radiography Used in Tuberculosis Case Finding
Herman E. Hilleboe, M.D., Russell H. Morgan, M.D., and Ira Lewis, M.D., Washington, D. C.

5:00 P. M. Convocation (Formal)

C. M. Hendricks, M.D., President-Elect, El Paso, Texas, *presiding*

Guest speaker to be announced

Awarding of Life Membership Certificates

Awarding of Fellowship Certificates

6:00 P. M. Cocktail Party

7:00 P. M. Annual Banquet (Formal)

President's Address:
Jay Arthur Myers, M.D., Minneapolis, Minnesota

Remarks, President-Elect:
Charles M. Hendricks, M.D., El Paso, Texas

College Chapter News

MISSOURI CHAPTER

The Missouri Chapter of the College held its annual meeting at the Jefferson Hotel, St. Louis, on March 24-25. The program presented at the meeting was published in the March-April issue of the College journal. The following officers were elected: President, Samuel Harrison Snider, M.D., Kansas City; Vice-President, William W. Buckingham, M.D., Kansas City; Secretary-Treasurer, Alexander Steiner, M.D., St. Louis.

The program for the meeting was arranged by Dr. H. I. Spector, St. Louis, Regent of the College for the district.

Alexander Steiner, M.D., *Secretary-Treasurer.*

NEW YORK STATE CHAPTER

The New York State Chapter held its annual meeting at the Hotel Pennsylvania, New York City, on the evening of May 2. It was a dinner meeting and the speakers of the evening were Dr. P. A. Herbut and Dr. Louis H. Clerf, F.C.C.P., Philadelphia, who jointly presented a paper entitled: "Cytology of Bronchial Secretions in the Diagnosis of Cancer".

Arthur Q. Penta, M.D., *Secretary-Treasurer.*

PENNSYLVANIA CHAPTER

The Pennsylvania Chapter of the College met jointly with the Laennec Society of Philadelphia, at the Bellevue-Stratford Hotel, Philadelphia, on April 3. The following program was presented:

Morning Scientific Session

Dr. Martin Sokoloff, President, Laennec Society, *presiding*

Rest in the Treatment of Pulmonary Tuberculosis,
Dr. R. S. Anderson, Superintendent and Medical Director,
Erie County Tuberculosis Hospital, Erie, Pa.

Penicillin and Streptomycin in the Treatment of Tuberculous and Non-Tuberculous Broncho-Pulmonary Disease
Dr. John Kolmer, Temple University

Tuberculous Tracheobronchitis
Dr. A. R. Judd, Hamburg, Pa.

Tuberculosis Control in the Army
Col. Esmond R. Long, M.C., U.S.A., and Director Henry Phipps Institute, University of Pennsylvania

Luncheon — Speakers

Dr. J. Winthrop, Peabody, Washington, D. C.,
Past-President, American College of Chest Physicians, and
Dr. C. Howard Marcy, Pittsburgh, Pennsylvania,
Medical Director, Tuberculosis League of Pittsburgh

Afternoon Scientific Session

Dr. Ross Childerhose, President, Pennsylvania Chapter, American College of Chest Physicians, *presiding*

Pulmonary Cysts
Dr. Burgess Gordon, Jefferson Medical College and Hospital, and White Haven Sanatorium

Clinical Features of Early Bronchogenic Carcinoma
Dr. Charles M. Norris, Chevalier Jackson Clinic, Temple University

Cytology of Bronchial Secretions in the Diagnosis of Cancer
Dr. T. A. Herbut (by invitation) and Dr. Louis H. Clerf, Jefferson Medical College and Hospital

Bronchoscopy in Some Types of Atelectasis
Dr. John S. Packard, Devitt's Camp, Allenwood, Pennsylvania

Differential Diagnosis of Broncho-Pulmonary Disease
Dr. W. Edw. Chamberlain, Temple University

Dinner

Toastmaster, Dr. Chevalier L. Jackson, Vice-President, Pennsylvania Chapter, American College of Chest Physicians, and Past-President, Laennec Society

Speaker, Dr. Richard Overholt, Boston, Massachusetts, Vice-President, American College of Chest Physicians,
Lung Resection in Broncho-Pulmonary Tuberculosis

The following officers were elected to hold office until the fall of 1947: President, Chevalier L. Jackson, M.D., Philadelphia; Vice-President, Henry A. Gorman, M.D., Hamburg; Secretary-Treasurer, Edward Lebovitz, M.D., Pittsburgh (Re-elected).

At the business meeting the following resolution was unanimously adopted:

> We, the undersigned, wish to present the following resolution to the members of the Pennsylvania Chapter of the American College of Chest Physicians.
>
> *Whereas,* the Sub-Board of Tuberculosis is inadequate, in as much as it does not fulfill the needs for proper certification of those physicians doing diseases of the chest.
>
> *Be it resolved,* that the Pennsylvania Chapter of the American College of Chest Physicians recommends to the Board of Regents, that they take proper steps to establish the American Board of Diseases of the Chest. Such a Board shall be incorporated in conformity with rules and regulations set forth by the Advisory Board for Medical Specialists and Council on Medical Education of the American Medical Association.
>
> *Signed:* Edward Lebovitz, M.D., C. Howard Marcy, M.D., Russell S. Anderson, M.D., Ross K. Childerhose, M.D., Chevalier L. Jackson, M.D., V. M. Leffingwell, M.D., John H. Bisbing, M.D.

Edward Lebovitz, M.D., *Secretary-Treasurer.*

WISCONSIN CHAPTER

The Milwaukee Section of the Wisconsin Chapter of the College will have as its next luncheon speaker, Dr. Mischa J. Lustok, F.C.C.P., who will talk on "Angular Roentgenography of the Pulmonary Apex." The Milwaukee Section of the Chapter holds monthly luncheon meetings to which speakers are invited.

Leon H. Hirsh, M.D., *Secretary-Treasurer.*

SPRING MEETING DATES

College Chapters	*State Medical Societies*
M A Y	
Arizona Chapter, May 1 Westward Ho Hotel, Phoenix.	Arizona State Medical Society May 2, 3, and 4.
New York State Chapter, May 2 Hotel Pennsylvania, New York City.	New York State Medical Society April 29-May 3.
Texas Chapter, May 6 Hotel Galvez, Galveston.	Texas State Medical Association May 6-9.
Ohio Chapter, May 8 Neil House, Columbus.	Ohio State Medical Society May 7, 8 and 9.
Illinois Chapter, May 13 Palmer House, Chicago.	Illinois State Medical Society May 14, 15 and 16.
New Jersey Chapter, May 21 Hotel Claridge, Atlantic City.	New Jersey State Medical Society May 21, 22 and 23.

COUNCIL ON EUROPEAN AFFAIRS ORGANIZED

In conformity with the policy of the College to establish a world society of qualified chest specialists, a Council on European Affairs was appointed by the President of the College. The Council members are:

Andrew L. Banyai, M.D., Milwaukee, Wisconsin, *Chairman*
Joseph C. Placak, M.D., Cleveland, Ohio, *Vice-Chairman*
Captain Robert E. Duncan, M.C., U.S.N., Bethesda, Maryland
Herman E. Hilleboe, M.D., Washington, D. C.
Chevalier L. Jackson, M.D., Philadelphia, Pennsylvania
Minas Joannides, M.D., Chicago, Illinois
A. A. Leonidoff, M.D., Poughkeepsie, New York
Major General S. U. Marietta, M.C., U.S.A., Washington, D. C.
Hugo Polderman, M.D., Waverly Hills, Kentucky
Hilary Roche, M.D., Montana, Switzerland
H. I. Spector, M.D., St. Louis, Missouri
Peter A. Theodos, M.D., Philadelphia, Pennsylvania
Luis Saye, M.D., Buenos Aires, Argentina

GREEK CHAPTER

The Greek Chapter of the College, with 15 Charter members, was organized in Athens on March 18, 1946. The following physicians, all residing in Athens, were admitted to the Chapter as Charter members:

Fellows: Dr. N. Oekonomopoulos, Dr. B. Papanicolaou, Dr. K. Katrakis, Dr. P. Chortis,

Associate Members: Dr. L. Muzas, Dr. T. Tsinikas, Dr. N. Yiannopoulos, Dr. G. Vakaloulis, Dr. J. Lameras, Dr. E. Joannides, Dr. C. Stephanopoulos, Dr. V. Malerdos, Dr. I. Papatestas, Dr. S. Ralli, and Dr. G. Papastathopoulos.

Dr. Peter A. Theodos, F.C.C.P., a member of the Council on European Affairs of the College, stationed in Athens with UNRRA, took the lead in organizing the Chapter. Dr. Theodos, with Dr. Oekonomopoulos, Professor of Tuberculosis, University of Athens, and Dr. Papanicolaou, Assistant Professor of Tuberculosis, are serving as an Examining Board to pass upon all new applicants.

MARYLAND - DISTRICT OF COLUMBIA CHAPTER ORGANIZED

The Maryland - District of Columbia Chapter of the College held its first meeting at the Hotel Belvedere, Baltimore, Maryland, on April 22. The scientific program presented at this meeting was published in the March-April issue of the journal. The Chapter was formally organized and the following officers were elected: President, William F. Rienhoff, Jr., M.D., Baltimore; Vice-President, Le Roy Dunn, M.D., Washington, D. C.; Secretary-Treasurer, I. B. Lyon, M.D., State Sanatorium, Maryland.

The members of the College in West Virginia were invited to become affiliated with the Chapter. Dr. George R. Maxwell, Governor of the College for West Virginia, and Dr. Merle D. Bonner, Governor of the College for North Carolina, attended the meeting, as well as members of the College from Virginia, Pennsylvania and other adjacent states.

The next meeting of the Chapter will be held in Washington, D. C., in the Fall of 1946, in connection with the Annual Meeting of the Medical Society of the District of Columbia.

I. B. Lyon, M.D., *Secretary-Treasurer.*

COLLEGE ACTIVITIES IN YUGOSLAVIA

Dr. Robert Neubauer (Lt. Col.), Lyublyana, Yugoslavia, has been appointed to membership on the College Council on European Affairs. Dr. Neubauer will be given the assignment of organizing a College chapter in Yugoslavia.

ANNOUNCEMENT

The American Bronchoesophagological Association will hold its 27th Annual Meeting at the Drake Hotel, Chicago, Ill., on Friday, May 31.

U. S. PUBLIC HEALTH REPORTS

U. S. Public Health Reports, March 1, 1946 is the first of a series of special issues containing articles devoted exclusively to tuberculosis control. The Tuberculosis Control Division of the U. S. Public Health Service will publish every month a special issue of Public Health Reports. Members of the American College of Chest Physicians will receive a copy of this special issue each month. A list of College membership

has been sent to the Publications Division of the U. S. Public Health Service, Washington, D. C., for this purpose. If you do not receive a copy of the special tuberculosis issue, send your name and address to the Publications Editor, Tuberculosis Control Division, U. S. Public Health Service, Washington 14, D. C., with a request that your name be placed on the list of College members.

ARMY MEDICAL LIBRARY

The Army Medical Library is desirous of building up its collection of portraits of persons prominent in medicine. The cooperation of the Fellows of the American College of Chest Physicians is requested in helping to expand this collection. Autographed photographs, preferably 8 x 11 inches in size, unmounted, should be sent to: The Director, Army Medical Library, 7th Street and Independence Avenue, S. W., Washington 25, D. C. Photographs should be plainly marked on the back with date and name of the subject.

The collection now includes 10,000 portraits of doctors of all periods and it is intended to expand the collection continuously. This collection will be of great value to everyone interested in American medicine.

COMMERCIAL SOLVENTS APPOINTS LAWRENCE W. SMITH, M.D. AS MEDICAL DIRECTOR

Lawrence W. Smith, M.D., well-known pathologist, is now associated with Commercial Solvents Corporation as Medical Director.

Previously, Dr. Smith was Professor of Pathology at Temple University School of Medicine and was Director of Laboratories at Temple University Hospital. He also worked extensively with the Lakeland Foundation on the development of therapeutic uses for chlorophyll and its derivatives in the cure of war wounds and burns.

Dr. Smith became instructor in pathology at Harvard University in 1920. In 1922 he went to the University of the Philippines at Manila as Professor of Pathology and Bacteriology. He returned to Harvard the following year as faculty instructor in pathology; he became Assistant Professor in 1926. In 1928 he joined the staff of Cornell University's Medical College, and was made Associate Professor in 1932.

Obituaries

CHARLES SAMUEL KIBLER

1889 - 1946

Dr. Charles Samuel Kibler, one of the outstanding chest physicians in the nation, died in his home in Colonia Solana, Arizona, on February 25, 1946. Death was due to a coronary thrombosis and came suddenly. His colleagues consider him a war casualty, due to overwork during the war period when there was a shortage of physicians.

Dr. Kibler was born in Newark, Ohio and was educated in Newark schools. He was graduated from Ohio State University in 1912 and the Rush Medical College of the University of Chicago in 1914. He interned for a year and a half in the Cook County Hospital, Chicago and practiced medicine for a year after that in Chicago. He was commissioned a captain in the U. S. Army during World War I. In 1921 Dr. Kibler went to Tucson, Arizona to join Dr. Meade Clyne and Dr. Samuel H. Watson in practice and had been affiliated with them since then in the Tucson Clinic. He was one of the leaders in the formation and operation of the medical staffs of St. Mary's, the Pima County Hospital, and last year was president of the first staff named for the Tucson Medical Center.

He was a Fellow of the American College of Chest Physicians and took an active part in the program of the College. Shortly before his death he had arranged the program for the annual meeting of the Arizona Chapter of the College at Phoenix, May 1, 1946. He also served as Regent of the College for the district. Dr. Kibler was active in the county and state medical societies; was a member of the American Heart Association and the American Medical Association; and was a certified member of the American Board of Internal Medicine. He was the author of many articles carried in national medical journals during the years of his practicing in Tucson. He was a member of the Old Pueblo Club, the Tucson Literary Club and was interested and active in civic affairs.

Howell Randolph, M.D.
Governor for Arizona.

BASCOMB LANIER CHIPLEY

1883 - 1945

Dr. Bascomb Lanier Chipley died from a heart attack in Brunswick, Maryland, while enroute from his home at Chillicothe, Ohio to New York City, May 13, 1945. Dr. Chipley was born in Phoenix, South Carolina; he attended the University of Georgia and later entered the University of Maryland Medical School where he received his degree in medicine in 1906. After graduation he practiced medicine at Coronaco, South Carolina. He served as a First Lieutenant, Medical Corps, U. S. Army, during World War I. He was appointed Assistant Surgeon at the Johnson City National Sanatorium, Johnson City, Tennessee and was transferred in 1923 to the National Home for Disabled Volunteer Soldiers, Danville, Illinois. Dr. Chipley served as First Assistant Physician at Valley View Sanatorium, Paterson, New Jersey, from December 1930 until March 1942, when he became Medical Director of the Mount Logan Tuberculosis Sanatorium at Chillicothe, Ohio, where he was serv-

ing at the time of his death. Dr. Chipley was a Fellow of the American College of Chest Physicians, and a member of the Ohio State Medical Association, American Medical Association, American Trudeau Society, American Society of Anesthetists and of the International College of Anesthetists.

Marcus W. Newcomb, M.D.
Governor for New Jersey

Book Reviews

Mass Radiography of the Chest, by Herman E. Hilleboe, M.D., Medical Director, Chief, Tuberculosis Control Division, U.S.P.H.S.; Professorial Lecturer on Tuberculosis Control, George Washington University; and Russell H. Morgan, M.D., Medical Officer-in-Charge Radiology Section, Tuberculosis Control Division, U.S.P.H.S.; Assistant Professor of Roentgenology, University of Chicago, 288 pages, 93 illustrations. Chicago: The Year Book Publishers, Inc., 1945. Cloth, $3.75.

Despite other arrangement of chapters, this book treats of three distinct phases of mass radiography: methods and procedures of mass surveys, mobile and other radiologic physics and technic, and clinical interpretation or diagnosis of x-ray films. Hence, it is a compendium of all procedures, technics and interpretations employed in or resulting from mass radiography of various population groups.

Departing from the foundation of the history of mass radiography, the authors present the primary objectives of tuberculosis control and then describe operative measures of mass radiography in any community. Case-finding, medical care, segregation of tuberculous patients, and rehabilitation of the tuberculous are correlated with activities of the health departments, local medical societies, sanatoria, voluntary tuberculosis associations and local welfare agencies. Three chapters are devoted to minute descriptions of records, filing systems and procedures used in mass radiography, as well as the study and care of persons found to have significant lesions.

In the second field covered by this volume, all of the multitude of technical questions regarding the actual roentgenology of mass radiography are fully and concisely answered. Available equipment installation designs, physical factors affecting equipment selection and the advisable technic in mass radiography are all given detailed consideration. One of the most fascinating chapters portrays the future developments in roentgenology and mass radiography.

Of vital concern and engrossing interest to the internist and general practitioner, as well as the roentgenologist, is the third subdivision of the book which deals with roentgen diagnosis of thoracic diseases. With 47 instructive x-ray film reproductions, the roentgenologist will find testimony of the effectiveness of such miniature x-ray films and clinicians will find an effective atlas or aid in differential diagnosis of thoracic pathology.

Much more adequately than any treatise previously published, this book covers its field and need. It is pleasingly written and is easy to read. Based as it is on years of experience in such work, it is the complete answer to the most inquiring and critical antagonists and protagonists of mass radiography.

E. J. Simons.

PULMONARY TUBERCULOSIS—A Handbook For Students and Practitioners: *by R. Y. Keers, M.D. (Edin.), F.R.F.P.S. (Glas.) and B. G. Rigden, M.R.C.S. (Eng.), L.R.C.P. (Lond.). Publishers, The Williams & Wilkins Company, 1945.*

The purpose of this book is to supply a very important and much neglected need in the anti-tuberculosis campaign, that is, it is intended to give to the physician, particularly as a medical student but practitioner as well, a practical working knowledge of the fundamentals of the diagnosis, treatment and control of tuberculosis—a difficult task in a handbook, yet, one well done. The authors realize that in lieu of a specific for the prevention or treatment of tuberculosis we are dependent upon education for these purposes—an education which must be universal and it is necessary to first educate the medical profession who, in turn, can most efficiently accomplish the general education.

The importance of recognizing tuberculosis as a systemic disease, of understanding the type of pulmonary pathology present and of treating the patient as an individual, is stressed. There are a number of excellent illustrations in the book. Most of these are reproductions of roentgenograms of the chest. Very wisely, in a book such as this, what is expected to be seen in the roentgenograms, is in most instances, outlined diagrammatically.

I would question the free administration of hypnotics. Unnecessary medication in the treatment of pulmonary tuberculosis, or of any condition, may have deleterious results. Sedatives for patients taking the cure for tuberculosis may be necessary, as a temporary expedient, to enable the patient to relax or while some patients are being trained to relax. When employed otherwise, they are usually a substitute for the physician's lack of control of his patient's mental processes. I also question the use of morphine in a tuberculous patient having pulmonary hemorrhage. The treatment of hemorrhage is largely one of controlling the patient, and at times, those near and dear to him. This can be done as well by measures having less dangerous potentialities.

As a whole, this book presents, in a concise manner, the effective and accepted methods of handling the tuberculous patient. The information it contains should be part of the knowledge and understanding of all medical graduates.

E. W. HAYES, M.D.

Positions Wanted and Available

POSITIONS WANTED

Wanted: Assistant Physician for tuberculosis sanatorium (Massachusetts). Must be graduate Class A school with some experience in tuberculosis. State age, professional history and other details first letter. Please address Box 138A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Medical Directorship desired by Fellow of the American College of Chest Physicians, which would afford a good medical opportunity for full time clinical work in tuberculosis and chest diseases. Fully experienced. For further particulars please address Box 220A, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois.

Chest specialist recently released from the service desires sanatorium position, preferably in California, New Mexico, or Arizona. Has specialized in tuberculosis work for past thirteen years. For further information please address Box 223A, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois.

POSITIONS AVAILABLE

Positions open in state department of public health. Physicians wanted who have had three years of experience in full time tuberculosis work, or with one year of experience in tuberculosis work and the rest in full time public health work. Salary $5,640 per annum, plus expenses of official travel, transportation, board and lodging. For further information please address Box 139A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Resident physician wanted to serve as medical director for 35-bed tax supported tuberculosis sanatorium in middle west. Salary and maintenance. Prefer young man experienced in sanatorium administration. For further particulars address Box 132A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Resident physician wanted for sanatorium in middle west. Salary $325 monthly; 3 room apartment completely furnished. Opportunity to learn or practice medicine and thoracic surgery under the most ideal conditions. For further information please address Box 130A, American College of Chest Physicians, 500 N. Dearborn Street, Chicago 10, Illinois.

Chest specialist in southwest desires assistant. Fine opportunity for participating in an established practice. For more complete information please write to Box 128A, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois.

Thoracic surgeon, part time institutional work and private practice at 250-bed tuberculosis hospital in Ohio. For additional information please address Box 131A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Position available for resident physician at 225-bed modern tuberculosis sanatorium in Hawaii. Requirements: Three years' sanatorium experience in the diagnosis and treatment of tuberculosis, including ability to read x-rays and prescribe proper regimes, American citizen, graduate of class A school, under 40 years of age. Minimum salary $520 monthly. For further particulars please address Box 133A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Resident physician needed in county tuberculosis hospital in Southern Texas. Previous tuberculosis training not necessary. Excellent opportunity for good training in tuberculosis and other chest diseases. For further information write Box 135A, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois.

County tuberculosis hospital in middle west in search of full time medical director who will have complete responsibility and treatment of patients who are hospitalized; the hospital also has an out-patient department. For further information write Box 136A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Medical superintendent needed in 140-bed state sanatorium in New England. For further particulars please write Box 137A, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois.